Devi, S. 1
09/284233

- key terms

FILE 'REGISTRY' ENTERED AT 15:53:55 ON 14 JUN 2000
E UREASE/CN 5
L1 165 SEA ABB=ON PLU=ON UREASE ?/CN

FILE 'CAPLUS' ENTERED AT 15:54:17 ON 14 JUN 2000
L2 2737 SEA ABB=ON PLU=ON (PATHOGEN OR ENTEROBACTER? OR ENTERO BACTER? OR SALMONELL?) AND (RECOMBINAN? OR ATTENUAT?)
L3 46 SEA ABB=ON PLU=ON L2 AND (L1 OR UREASE OR MIMOTOP? OR SECRET?(W)(POLYPEPTIDE OR POLY PEPTIDE) OR ALPA OR ALPB OR ALP(W)(A OR B) OR HELICOBACTER?)
L4 28 SEA ABB=ON PLU=ON L3 AND (VACCIN? OR IMMUNIS? OR IMMUNIZ?)

L4 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:282541 CAPLUS
TITLE: **Immunization** with **recombinant** **Helicobacter** pylori **urease** in specific-**pathogen**-free rhesus monkeys (Macaca mulatta)
AUTHOR(S): Solnick, Jay V.; Canfield, Don R.; Hansen, Lori M.; Torabian, Sima Z.
CORPORATE SOURCE: Departments of Internal Medicine (Division of Infectious Diseases) and Medical Microbiology and Immunology, Davis School of Medicine, University of California, Davis, CA, 95616, USA
SOURCE: Infect. Immun. (2000), 68(5), 2560-2565
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Immunization** with **urease** can protect mice from challenge with **Helicobacter** pylori, though results vary depending on the particular **vaccine**, challenge strain, and method of evaluation. Unlike mice, rhesus monkeys are naturally colonized with H. pylori and so may provide a better est. of **vaccine** efficacy in humans. The purpose of this study was to examine the effectiveness of H. pylori **urease** as a **vaccine** in specific-**pathogen** (H. pylori)-free rhesus monkeys. Monkeys raised from birth and documented to be free of H. pylori were **vaccinated** with orogastric (n = 4) or i.m. (n = 5) **urease**. Two control monkeys were sham **vaccinated**. All monkeys were challenged with a rhesus monkey-derived strain of H. pylori, and the effects of **vaccination** were evaluated by use of quant. cultures of gastric tissue, histol., and measurement of serum IgG (IgG) and salivary IgA. Despite a humoral immune response, all monkeys were infected after H. pylori challenge, and there were no differences in the d. of colonization. **Immunization** with **urease** therefore does not fully protect against challenge with H. pylori.

Searcher : Shears 308-4994

An effective **vaccine** to prevent H. pylori infection will require different or more likely addnl. antigens, as well as improvements in the stimulation of the host immune response.

REFERENCE COUNT: 34
REFERENCE(S):
(3) Corthesy-Theulaz, I; Infect Immun 1998, V66, P581 CAPLUS
(5) Drazek, E; J Clin Microbiol 1994, V32, P1799 CAPLUS
(7) Dubois, A; Infect Immun 1998, V66, P4340 CAPLUS
(9) Dunn, B; Clin Microbiol Rev 1997, V10, P720 CAPLUS
(11) Ermak, T; J Exp Med 1998, V188, P2277 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:213598 CAPLUS
TITLE: Pilot study of phoP/phoQ-deleted **Salmonella** enterica serovar typhimurium expressing **Helicobacter** pylori **urease** in adult volunteers
AUTHOR(S): Angelakopoulos, Haroula; Hohmann, Elizabeth L.
CORPORATE SOURCE: Infectious Disease Division, Department of Medicine, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: Infect. Immun. (2000), 68(4), 2135-2141
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Attenuated Salmonella** enterica serovar Typhi has been studied as an oral **vaccine** vector. Despite success with **attenuated** S. enterica serovar Typhimurium vectors in animals, early clin. trials of S. enterica serovar Typhi expressing heterologous antigens have shown that few subjects have detectable immune responses to vectored antigens. A previous clin. study of phoP/phoQ-deleted S. enterica serovar Typhi expressing **Helicobacter** pylori **urease** from a multicopy plasmid showed that none of eight subjects had detectable immune responses to the vectored antigen. In an attempt to further define the variables important for engendering immune responses to vectored antigens in humans, six volunteers were inoculated with 5 .times. 107 to 8 .times. 107 CFU of phoP/phoQ-deleted S. enterica serovar Typhimurium expressing the same antigen. Two of the six volunteers had fever; none had diarrhea, bacteremia, or other serious side effects. The volunteers were more durably colonized than in previous studies of phoP/phoQ-deleted S. enterica serovar Typhi. Five of the six volunteers seroconverted to S. enterica serovar

Typhimurium antigens and had strong evidence of anti-**Salmonella** mucosal immune responses by enzyme-linked immunospot studies. Three of six (three of five who seroconverted to **Salmonella**) had immune responses in the most sensitive assay of **urease**-specific Ig prodn. by blood mononuclear cells in vitro. One of these had a fourfold or greater increase in end-point Ig titer in serum vs. **urease**. **Attenuated** S. enterica serovar Typhimurium appears to be more effective than S. enterica serovar Typhi for engendering immune responses to **urease**. Data suggest that this may be related to a greater stability of antigen-expressing plasmid in S. enterica serovar Typhimurium and/or prolonged intestinal colonization. Specific factors unique to nontyphoidal **salmonellae** may also be important for stimulation of the gastrointestinal immune system.

REFERENCE COUNT: 30
REFERENCE(S):
(4) DiPetrillo, M; Vaccine 1999, V18, P449 CAPLUS
(7) Galan, J; Curr Opin Microbiol 1999, V2, P46 CAPLUS
(14) Hone, D; Infect Immun 1988, V56, P1326 CAPLUS
(15) Hornick, R; N Engl J Med 1970, V283, P686 CAPLUS
(16) Ibrahim, G; J Clin Microbiol 1985, V22, P1040 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:175939 CAPLUS
DOCUMENT NUMBER: 132:217984
TITLE: **Attenuated Salmonella** pathogenicity island 2 mutants as antigen carriers
INVENTOR(S): Hensel, Michael; Guzman, Carlos Alberto; Medina, Eva; Apfel, Heiko; Hueck, Christoph
PATENT ASSIGNEE(S): Creatogen Biosciences G.m.b.H., Germany
SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014240	A2	20000316	WO 1999-EP6514	19990903

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,

Searcher : Shears 308-4994

ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 1998-116827 19980904

AB The present invention relates to **vaccines**, in particular, to an **attenuated** gram-neg. cell comprising the pathogenicity island 2 (SPI2) locus, wherein at least one gene of the SPI2 locus is inactivated. The type III secretion system of the SPI2 locus comprising effector (sse), chaperon (ssc), and regulatory (ssr) genes of **Salmonella** typhimurium DT104 is characterized by sequence and genomic organization. Inactivation results in an **attenuation**/redn. of virulence compared to the wild type of said cell. The **attenuated** gram-neg. cells can be used as a **vaccine** carrier for the presentation of an antigen to a host, wherein said cell comprises at least one heterologous nucleic acid mol. comprising a nucleic acid sequence coding a viral, bacterial, or tumor antigen.

L4 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:98814 CAPLUS
DOCUMENT NUMBER: 132:165125
TITLE: Gastrointestinal bacterial antibody factories
INVENTOR(S): Fahl, William E.; Letchworth, Geoffrey J.; Mueller, Gerald C.; Savage, Adam K.; Loo, Deborah
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006764	A1	20000210	WO 1999-US17296	19990729

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-94697 19980730

AB Neonates during their first thirty days of life are particularly susceptible to **pathogens** because their immune system is not yet fully functional. Adults may also be unusually susceptible to **pathogens** when their immune system has been compromised by disease or when they have been acutely exposed to a bolus of GI **pathogen**. The invention provides a method of **immunizing** neonates and adults to **pathogens** by orally administering **recombinant** probiotic bacteria that express antibodies to the **pathogens**. These **recombinant** bacteria may be optionally administered with antibodies immunol. specific to the **pathogens**. The invention further provides a compn. of **recombinant** probiotic bacteria that express antibodies to **pathogen**, and a method to use this compn. to **immunize** neonates and adults.

REFERENCE COUNT: 7

REFERENCE(S):
(1) Green; US 5637677 A 1997 CAPLUS
(2) Greenberg; US 4571385 A 1986
(3) Lee; US 5733540 A 1998
(4) Majnarich; US 5895758 A 1999
(7) Snyder; US 4956452 A 1990 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:775344 CAPLUS

DOCUMENT NUMBER: 132:263803

TITLE: Safety and immunogenicity of phoP/phoQ-deleted **Salmonella** typhi expressing **Helicobacter** pylori **urease** in adult volunteers

AUTHOR(S): DiPetrillo, Melissa D.; Tibbetts, Timothy; Kleanthous, Harry; Killeen, Kevin P.; Hohmann, Elizabeth L.

CORPORATE SOURCE: Infectious Disease Division, Massachusetts General Hospital, Boston, MA, 02114, USA

SOURCE: Vaccine (1999), 18(5-6), 449-459
CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Salmonella** typhi Ty800, deleted for the **Salmonella** phoP/phoQ virulence regulon has been shown to be a safe and immunogenic single dose oral typhoid fever **vaccine** in volunteers. This promising **vaccine** strain was modified to constitutively express a heterologous protein of Gram neg. bacterial origin, **Helicobacter** pylori **urease** subunits A and B, yielding S. typhi strain Ty1033. Seven volunteers received single oral doses of .gtoreq. 1010 colony forming units of Ty1033;

an eighth volunteer received two doses 3 mo apart. Side effects were similar to those obsd. previously in volunteers who received the unmodified vector Ty800. All volunteers had strong mucosal immune responses to **vaccination** as measured by increases in IgA-secreting cells in peripheral blood directed against S. typhi antigens. Seven of eight volunteers had convincing seroconversion as measured by increases in serum IgG directed against S. typhi flagella and lipopolysaccharide antigens by ELISA. No volunteer had detectable mucosal or humoral immune responses to the **urease** antigen after **immunization** with single doses of Ty1033. A subset of three volunteers received an oral booster **vaccination** consisting of **recombinant** purified H. pylori **urease** A/B and E. coli heat labile toxin adjuvant 15 days after **immunization** with Ty1033. None of three had detectable humoral or mucosal immune responses to **urease**. Expression of a stable immunogenic protein in an appropriately **attenuated** S. typhi vector did not engender detectable mucosal or systemic antibody responses; addnl. work will be needed to define variables important for immunogenicity of heterologous antigens carried by live S. typhi vectors in humans.

REFERENCE COUNT: 33

REFERENCE(S):

(1) Corthesy-Theulaz, I; Infect Immun 1998, V66, P581 CAPLUS
(2) Coynault, C; Molecular Microbiology 1996, V22, P149 CAPLUS
(4) Donnenberg, M; Infect Immun 1991, V59, P4310 CAPLUS
(5) Dubois, A; Infect Immun 1998, V66, P4340 CAPLUS
(6) Faulde, M; Electrophoresis 1993, V14, P945 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:736886 CAPLUS
DOCUMENT NUMBER: 131:347498
TITLE: Cytotoxin-based biological containment system based on protein degradation for environmental pollution clean-up
INVENTOR(S): Gerdes, Kenn; Gotfredsen, Marie; Gronlund, Hugo; Pedersen, Kim; Kristoffersen, Peter
PATENT ASSIGNEE(S): GXBiosystems A/S, Den.
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958652	A2	19991118	WO 1999-DK258	19990507
WO 9958652	A3	20000120		

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9935963	A1	19991129	AU 1999-35963	19990507
PRIORITY APPLN. INFO.:			DK 1998-627	19980507
			US 1998-85067	19980512
			WO 1999-DK258	19990507

AB Method of conditionally controlling the survivability of a **recombinant** cell population and of contg. such cells to an environment or contg. replicons to a host cell is based on the use of protein killer systems including the E. coli relBE locus and similar systems found in Gram-neg. (**Enterobacteriaceae**, Hemophilus, Vibrionaceae, Pseudomonadaceae, **Helicobacter**, and Synechosystis) and Gram-pos. bacteria (Bacillaceae and Mycobacterium and Bacillus thuringiensis) and Archaea. Such system are generally based on a cytotoxin polypeptide and an antitoxin or antidote polypeptide that in contrast to the cytotoxin is degradable by proteases. In this system the regulation of the relE gene is stochastically regulated. Here the promoter is invertible. This involves flanking the regulatory sequence with repeat sequences where at least part of the regulatory sequence is recombinationally excised. Expression of genes of interest may include an enzyme or an immunol. active peptide or a pesticide or a pharmaceutically active gene product. Methods for post-segregationally stabilizing a plasmid in a microbial host cell involves integration a plasmid with regulated expression of a first kind of protein with a toxic effect and a gene coding for a second kind of polypeptide with an antitoxin effect. This first kind of polypeptide may inhibit translation. The antitoxin is capable of being degraded at a higher rate than the first polypeptide. Screening for daughter cells in employed where one that does not receive at least one copy of the plasmid is killed as a result of faster degrdn. The **recombinant** cells are useful as **vaccines**, pollutant degrading organisms or as biol. pest control organisms e.g. expressing B. thuringiensis cryst. proteins.

L4 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:673792 CAPLUS

DOCUMENT NUMBER: 132:2664
TITLE: Defining B cell epitopes of ovalbumin for the C57BL/6 mice **immunized** with **recombinant** Mycobacterium smegmatis
AUTHOR(S): Kim, Hyo Joon; Lee, Yang Min; Hwang, Joon Sung; Won, Hoshik; Kim, Bok Hwan
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, College of Sciences, Hanyang University, Kyunggi, 425-791, S. Korea
SOURCE: J. Biochem. Mol. Biol. (1999), 32(5), 461-467
CODEN: JBMBE5; ISSN: 1225-8687
PUBLISHER: Springer-Verlag Singapore Pte. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Recombinant** Mycobacterium smegmatis expressing ovalbumin was used to **immunize** C57BL/6(H-2b) mice, and the humoral immunity against **recombinant** ovalbumin was analyzed. Antibodies were purified by denatured ovalbumin-conjugated affinity chromatog. The epitopes of the antibodies were screened with a random peptide library displayed on the tip of fUSE5 filamentous phage pIII minor coat proteins. Two peptides, IRLADR and SPGAEV, were selected predominantly by the recognition of purified antibodies using biopanning methods. The compn. of the peptide sequence with the primary structure of OVA revealed that the peptide sequence analogizes to INEAGR, part of the 323ISQAVHAAHAEINEAGR339 sequence previously reported as the antigenic determinant for murine B and also Th cell epitopes (I-Ad binding). Also, the structures of these **mimotopes** obtained from restrained mol. dynamic computations resulted in the formation of a .beta.-turn proven to be a secondary structure of the parent peptide within the ovalbumin mol., enabling us to confirm the structural similarity. This study demonstrates that **immunization** with **recombinant** M. smegmatis can generate neutralizing antibodies identical with those induced by the administration of natural antigenic proteins and supports the potential use of mycobacteria as **vaccine** delivery vehicles.

REFERENCE COUNT: 34
REFERENCE(S):
(1) Aldovini, A; Nature 1991, V351, P479 CAPLUS
(2) Bazin, H; Immunology 1976, V30, P679 CAPLUS
(3) Bennett, S; J Exp Med 1998, V188, P1977 CAPLUS
(4) Buus, S; Proc Natl Acad Sci USA 1986, V83, P3968 CAPLUS
(5) Carcamo, J; Proc Natl Acad Sci USA 1998, V95, P11146 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:595191 CAPLUS
Searcher : Shears 308-4994

DOCUMENT NUMBER: 131:210989
TITLE: Gene dnaB encoding a replicative helicase of Staphylococcus aureus
INVENTOR(S): May, Earl W.; Earnshaw, David L.; Mcdevitt, Damien
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline Beecham, Plc
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9946275	A1	19990916	WO 1999-US5286	19990310

W: JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1998-38909 19980312

AB The invention provides dnaB polypeptides and polynucleotides encoding dnaB polypeptides and methods for producing such polypeptides by **recombinant** techniques. The dnaB gene product of Staphylococcus aureus is 466 amino acids in length and related by amino acid sequence homol. to helicases from S. pneumoniae, Escherichia coli, Bacillus subtilis, **Helicobacter** pylori, Synchocystis, Mycobacterium, Haemophilus influenzae, and **Salmonella** typhimurium polypeptides. Also provided are methods for utilizing dnaB polypeptides to screen for antibacterial compds.

REFERENCE COUNT: 4
REFERENCE(S):
(1) Ngo; The Protein Folding Problem and Tertiary Structure Prediction 1994, P433 CAPLUS
(2) Ogasawara, N; Database Genbank 1999
(3) Rudinger, J; Peptide Hormones P1
(4) Smithkline Beecham Corporation; WO 9730070 A1 1997 CAPLUS

L4 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:529264 CAPLUS
DOCUMENT NUMBER: 131:169280
TITLE: Antigen library **immunization**
INVENTOR(S): Punnonen, Juha; Bass, Steven H.; Whalen, Robert Gerald; Howard, Russell; Stemmer, Willem P. C.
PATENT ASSIGNEE(S): Maxygen, Inc., USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2

Searcher : Shears 308-4994

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941383	A1	19990819	WO 1999-US2944	19990210
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9932891	A1	19990830	AU 1999-32891	19990210
PRIORITY APPLN. INFO.:			US 1998-21769	19980211
			US 1998-PV74294	19980211
			US 1998-PV105509	19981023
			US 1998-74294	19980211
			US 1998-105509	19981023
			WO 1999-US2944	19990210

AB This invention is directed to antigen library **immunization**, which provides methods for obtaining **recombinant** multivalent antigens having improved properties for therapeutic and other uses. The methods are useful for obtaining improved antigens that can induce an immune response against **pathogens**, cancer, and other conditions, as well as antigens that are effective in modulating allergy, inflammatory and autoimmune diseases.

REFERENCE COUNT: 3
REFERENCE(S):
(1) Affymax Technologies N V; WO 9720078 A 1997
(2) Crameri, A; Nature 1998, V391(6664), P288 CAPLUS
(3) Gritz, L; US 5691170 A 1997

L4 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:511311 CAPLUS
DOCUMENT NUMBER: 131:143515
TITLE: Peptide **mimotopes** of carbohydrate antigens
INVENTOR(S): Kieber-Emmons, Thomas
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940433	A1	19990812	WO 1999-US2405	19990204
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9926575	A1	19990823	AU 1999-26575	19990204
PRIORITY APPLN. INFO.:			US 1998-PV73690	19980204
			US 1998-73690	19980204
			WO 1999-US2405	19990204

AB Methods of prepg. a peptide and antigenic antibodies which mimic an antigenic carboyhdrate are disclosed. The method comprises the steps of identifying a peptide sequence which is immunogenically cross reactive an antigenic carbohydrate and synthesizing a peptide or **recombinant** antibody which comprises the peptide sequence. Methods of generating an immune response against a **pathogen** or tumor cell in an individual using such peptides, **recombinant** antibodies comprising such peptide, or DNA **vaccines** live **attenuated vaccines**, or **recombinant vaccines** that encode such peptides are disclosed. Methods of enhancing binding of anti-antigenic carbohydrate antibodies to the antigenic carbohydrate in an individual are disclosed. The methods comprise administering to an individual anti-antigenic carbohydrate antibodies and a peptide which mimics the antigenic carbohydrate. Methods of inhibiting binding of a ligand to a receptor which is an antigenic carbohydrate are disclosed. The methods comprise administering to an individual a peptide which mimics an antigenic carbohydrate. Methods of identifying peptide sequences which can induce an immune response against two or more different **pathogens** are disclosed. Novel compns. are disclosed.

REFERENCE COUNT: 8

REFERENCE(S):

(3) Luo, P; Molecular Immunology 1998, V35, P865 CAPLUS
(4) Miller; US 5817748 A 1998 CAPLUS
(5) Oldenburg, K; Proc Natl Acad Sci USA 1992, V89, P5393 CAPLUS
(6) Valadon, P; J Mol Biol 1996, V261, P11 CAPLUS
(7) Westerink, M; Proc Natl Acad Sci USA 1995, V92, P4021 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:70376 CAPLUS

DOCUMENT NUMBER: 130:144164

TITLE: Detoxified immunogenic .beta.-toxin derivative

as a Clostridium perfringens **vaccine**

INVENTOR(S): Sergers, Ruud Philip Antoon Maria; Waterfield, Nicolas Robin; Frandsen, Peer Lyng; Wells, Jeremy Mark

PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.

SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 892054	A1	19990120	EP 1998-202032	19980617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2235445	AA	19981220	CA 1998-2235445	19980618
AU 9873087	A1	19981224	AU 1998-73087	19980619
ZA 9805393	A	19990217	ZA 1998-5393	19980619
JP 11103872	A2	19990420	JP 1998-210185	19980619
CN 1215729	A	19990505	CN 1998-103183	19980619
BR 9802361	A	20000111	BR 1998-2361	19980622

PRIORITY APPLN. INFO.: EP 1997-201888 19970620

AB The present invention relates to detoxified immunogenic derivs. of Clostridium perfringens .beta.-toxin or an immunogenic fragment thereof that have as a characteristic that they carry a mutation in the .beta.-toxin amino acid sequence, not found in the wild-type .beta.-toxin amino acid sequence. Those regions of the .beta.-toxin that are particularly suitable are those that form a transition domain between neutral and hydrophilic parts of the protein; thus, suitable target regions for mutations are located at position 62, 182, 197, between 80-103, 145-147, 281-291 relative to the peptide leader methionine, and the region downstream of the unique cysteine-292. The invention also relates to genes encoding such .beta.-toxins, as well as to expression systems expressing such .beta.-toxins. Expression plasmids were constructed suitable for Lactococcus lactis. Moreover, the invention relates to bacterial expression systems expressing a native .beta.-toxin. Finally, the invention relates to **vaccines** based upon detoxified immunogenic derivs. of Clostridium perfringens .beta.-toxin, and methods for the prepn. of such **vaccines**. Pigs responded to **vaccination** with the genetically modified .beta.-toxin by producing .beta.-toxin-inhibiting anti-.beta.-antibodies.

REFERENCE COUNT: 7
REFERENCE(S):
(1) Hunter; Infection and Immunity 1993, V61(9), P3958 CAPLUS
(2) Pasteur Institut; WO 9517521 A 1995
(3) Sakurai; Infection and Immunity 1977,

V18(3), P741 CAPLUS
(4) Secr Defence; WO 9323543 A 1993
(5) Secr Defence Brit; WO 9734001 A 1997
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:32017 CAPLUS
DOCUMENT NUMBER: 130:94472
TITLE: **Attenuated** Vibrio cholerae strains
INVENTOR(S): Fontana, Mariarita; Pizza, Mariagrazina; Rappuoli, Rino
PATENT ASSIGNEE(S): Chiron S.P.A., Italy
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 887403	A2	19981230	EP 1998-305060	19980626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			GB 1997-13664	19970627
			GB 1997-22435	19971023

AB The present invention relates to **attenuated** strains of Vibrio cholerae and their use as carrier agents for antigens in the mammalian body. The **attenuated** strains of the present invention can be used as carriers for both heterologous and homologous antigens. The strains of the present invention colonize the human intestine efficiently yet safely and generate antibodies with high bactericidal or anti-viral activity.

L4 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:8105 CAPLUS
DOCUMENT NUMBER: 130:71518
TITLE: Live **attenuated** bacterial **vaccines** containing a modified iron uptake fur gene
INVENTOR(S): Baldwin, Thomas John; Borriello, Saverio Peter; Palmer, Helen Mary
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856901	A2	19981217	WO 1998-GB1683	19980609
WO 9856901	A3	19990318		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9880268	A1	19981230	AU 1998-80268	19980609
EP 996712	A2	20000503	EP 1998-928436	19980609

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.:	GB 1997-11964	19970609
	WO 1998-GB1683	19980609

AB An **attenuated** bacterium in which the native fur gene, or homolog thereof, is modified such that the expression of the fur gene product, or homolog thereof, is regulated independently of the iron concn. in the environment of the bacterium, is suitable for use as a live **vaccine**. This has important implications in the manuf. of live **vaccines** since the increased expression of the protective antigens during the manuf. process will increase the efficacy of the live **vaccine** when administered to an animal or human subject. For alterations in the fur gene it is essential not to have a complete knockout mutant since this may be lethal. Thus, the fur gene may be placed under the control of another promoter which can be switched on or off independently of the factors (iron) which normally controls fur expression. Preferably, the bacterium is also **attenuated** by mutation of at least one gene essential for the prodn. of a metabolite or catabolite not produced by a human or animal; such mutations may be in an aro gene such as an aroB gene and/or aroL gene and/or a gene of the pur or pyr pathways. The bacterium may be, in particular, Neisseria meningitidis.

L4 ANSWER 14 OF 28 CAPLUS

ACCESSION NUMBER:	1998:684969 CAPLUS
DOCUMENT NUMBER:	129:289183
TITLE:	Virulence-**attenuated** poxR mutant bacteria and their use as **vaccines**
INVENTOR(S):	Kaniga, Kone; Sundaram, Preeti
PATENT ASSIGNEE(S):	Megan Health, Inc., USA
SOURCE:	PCT Int. Appl., 67 pp.
	CODEN: PIXXD2

Searcher : Shears 308-4994

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844120	A1	19981008	WO 1998-US6406	19980331
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9868753	A1	19981022	AU 1998-68753	19980331
EP 972046	A1	20000119	EP 1998-914391	19980331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-829402	19970331
			WO 1998-US6406	19980331

AB Disclosed are bacteria having virulence **attenuated** by a mutation to the gene poxR and a method of producing them. Such bacteria are useful for inducing an immune response in an animal or human against virulent forms of the bacteria with reduced risk of a virulent infection and as an alternative to normally virulent bacteria as research tools. In a preferred embodiment, poxR **attenuated** bacteria can be used as a **vaccine** to induce immunoprotection in an animal against virulent forms of the bacteria. The disclosed bacteria can also be used as hosts for the expression of heterologous genes and proteins, or to deliver DNA for genetic **immunization**, or to deliver and present heterologous antigens to the immune system of an animal, leading to improved stimulation of an immune response to the antigens. It has been discovered that bacteria harboring a poxR mutation has significantly reduced virulence. Also disclosed is the nucleotide sequence of the poxR gene from **Salmonella** typhimurium, and the amino acid sequence of the encoded protein. The encoded protein has 325 amino acids and has significant sequence similarity to class-II lysyl-tRNA synthetases.

L4 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:683750 CAPLUS
DOCUMENT NUMBER: 130:94134
TITLE: **Immunization** of BALB/c mice with **Helicobacter urease** B induces a T helper 2 response absent in **Helicobacter** infection
AUTHOR(S): Saldinger, Pierre F.; Porta, Nadine; Launois, Pascal; Louis, Jacques A.; Waanders, Gary A.; Bouzourene, Hanifa; Michetti, Pierre; Blum, Andre L.; Corthesy-Theulaz, Irene E.
CORPORATE SOURCE: Division of Gastroenterology, Department of

Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switz.
SOURCE: Gastroenterology (1998), 115(4), 891-897
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Infection with **Helicobacter** induces a T helper type 1 response in mice and humans. Mice can be cured or protected from infection with **Helicobacter** by mucosal **immunization** with **recombinant** H. pylori **urease** B subunit (rUreB). This study characterizes the immune response of infected mice **immunized** with rUreB. BALB/c mice were infected with H. felis. Two weeks later, they were orally **immunized** four times with rUreB and cholera toxin (CT) at weekly intervals. Controls were only infected or sham-**immunized** with CT. Animals were killed at various times after **immunization**. Splenic CD4+ cells were obtained and cultured in vitro with rUreB to evaluate antigen-specific proliferation and induction of interferon gamma and interleukin 4 secretion. All rUreB-**immunized** mice (n = 8) were cured from infection 3 wk after the fourth **immunization**. **Immunization** induced a proliferative response of splenic CD4+ cells, a progressive decrease in interferon gamma secretion, and a concomitant increase in interleukin 4 secretion after each **immunization**. A simultaneous increase in rUreB specific serum IgG1 levels was obsd. in infected/**immunized** mice. In BALB/c mice, therapeutic mucosal **immunization** with rUreB induces progressively a Th2 CD4+ T cell response resulting in the elimination of the **pathogen**.

REFERENCE COUNT: 34
REFERENCE(S):
(1) Bourguin, I; Infect Immun 1993, V61, P2082 CAPLUS
(9) D'Elios, M; J Immunol 1997, V158, P962 CAPLUS
(10) Ernst, P; Curr Opin Gastroenterol 1995, V11, P512 CAPLUS
(12) Favre, N; J Immunol Methods 1993, V164, P213 CAPLUS
(13) Ferrero, R; Gastroenterology 1997, V113, P185 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:341583 CAPLUS
DOCUMENT NUMBER: 129:64083
TITLE: **Helicobacter** polypeptides and corresponding polynucleotide molecules for use in **vaccination** methods to prevent or

treat infection

INVENTOR(S): Haas, Rainer; Kleanthous, Harold; Tomb, Jean-Francois; Miller, Charles; Al-Garawi, Amal; Odenbreit, Stefan; Meyer, Thomas; et al.

PATENT ASSIGNEE(S): Merieux Oravax Societe en Nom Collectif Pasteur Merieux Serums et Vaccins S., Fr.; Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V. Berlin; Human Genome Sciences, Inc.

SOURCE: PCT Int. Appl., 365 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9821225	A1	19980522	WO 1997-US21353	19971114
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9852662	A1	19980603	AU 1998-52662	19971114
WO 9843478	A1	19981008	WO 1998-US6371	19980401
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9870995	A1	19981022	AU 1998-70995	19980401
EP 977482	A1	20000209	EP 1998-917972	19980401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1996-749051	19961114
US 1997-831309	19970401
US 1997-833457	19970401
US 1997-834705	19970401
US 1997-881227	19970624
US 1997-902615	19970729

Searcher : Shears 308-4994

WO 1997-US21353 19971114
WO 1998-US6371 19980401

AB The invention provides **Helicobacter** polypeptides that can be used in **vaccination** methods for preventing or treating **Helicobacter** infection, and polynucleotides that encode these polypeptides. A representative gene library was constructed in Escherichia coli, in which target genes encoding exported H. pylori proteins were efficiently tagged by transposon TnMax9. Sequences of clones using the transposon shuttle mutagenesis methods were used to identify intact genes, lacking inserted transposons, in the H. pylori genome. Methods are also provided for (1) identification of signal sequences and primer design for amplification of genes lacking signal sequences, (2) cloning of H. pylori DNA in a vector that provides a histidine tag and prodn. and purifn. of the resulting His-tagged fusion proteins, (3) cloning DNA encoding the polypeptides of the invention so that they can be produced without His-tags, (4) purifn. of **recombinantly** produced polypeptides, (5) obtaining the nucleic acids of the invention from the deposited clones, and (6) purifn. of **recombinant** H. pylori antigen GHPO 1190. Eighty-five different gene sequences and the deduced amino acid sequences of their encoded proteins are provided.

L4 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:251195 CAPLUS
DOCUMENT NUMBER: 128:307520
TITLE: **Helicobacter** pylori live **vaccine**
INVENTOR(S): Meyer, Thomas F.; Haas, Rainer; Zhengxin, Yan; Gomez-Duarte, Oscar; Lucas, Bernadette
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V., Germany; Meyer, Thomas F.; Haas, Rainer; Zhengxin, Yan; Gomez-Duarte, Oscar; Lucas, Bernadette
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816552	A1	19980423	WO 1997-EP4744	19970901

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,

TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

EP 835928	A1	19980415	EP 1996-116337	19961011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
EP 931093	A1	19990728	EP 1997-940148	19970901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, FI				
BR 9713254	A	19991103	BR 1997-13254	19970901
NO 9901692	A	19990604	NO 1999-1692	19990409
PRIORITY APPLN. INFO.:			EP 1996-116337	19961011
			WO 1997-EP4744	19970901

AB The present invention relates to novel **recombinant** live **vaccines**, which provide protective immunity against an infection by **Helicobacter** pylori and a method of screening H. pylori antigens for optimized **vaccines**. Thus, **Salmonella** typhimurium expressing ureA/ureB subunits of **Helicobacter** pylori was constructed and used as **vaccine** to elicit protective immunity against H. pylori infection.

L4 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:236314 CAPLUS
DOCUMENT NUMBER: 128:307512
TITLE: **Recombinant** coryneform bacteria expressing antigens of pathogenic microorganisms for use as **vaccines**
INVENTOR(S): Kobayashi, Mikio; Yukawa, Hideaki
PATENT ASSIGNEE(S): Mitsubishi Chemical Industries Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10099077	A2	19980421	JP 1996-256860	19960927

AB Disclosed of non-pathogenic coryneform bacteria for the expression of antigens of pathogenic microorganisms for use as **vaccines** in mammalian animals such as human. Expression of gene Hsp40 of Staphylococcus aureus or Bordetella pertussis in transgenic Brevibacterium flavum strain MJ-233 was demonstrated.

L4 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:126362 CAPLUS
DOCUMENT NUMBER: 128:191580

TITLE: Treatment and prevention of **Helicobacter** infection with **recombinant** **Helicobacter** catalase
INVENTOR(S): Doidge, Christopher Vincent; Lee, Adrian; Radcliff, Fiona Jane; Hazell, Stuart Lloyd
PATENT ASSIGNEE(S): CSL Limited, Australia; University of New South Wales
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9806853	A1	19980219	WO 1997-AU515	19970814
W: AU, CA, JP, KR, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6005090	A	19991221	US 1996-695987	19960815
AU 9737623	A1	19980306	AU 1997-37623	19970814
PRIORITY APPLN. INFO.:			US 1996-695987	19960815
			AU 1994-6124	19940608
			WO 1995-AU335	19950608
			WO 1997-AU515	19970814

AB An antigenic prepn. for use in the treatment or prevention of **Helicobacter** infection in a mammalian host, comprises **recombinant** catalase enzyme of **Helicobacter** bacteria, particularly **recombinant** catalase enzyme of H. pylori or H. felis, or an immunogenic fragment. Thus, an antigenic prepn. of catalase is used in a **vaccine** compn. for oral administration which includes a mucosal adjuvant such as cholera toxin. **Helicobacter** catalase may be administered as the sole active immunogen in a **vaccine** compn. or expressed by alive vector. Thus, catalase was purified from H. pylori (clin. strain 921023) and shown to **immunize** mice against infection by H. pylori or H. felis. E. coli clones expressing catalase from 2 different isolates of H. pylori (isolate RU1 and isolate 921023) were also characterized, and **recombinant** catalase shown to be an effective protective antigen for **immunization** against H. pylori infection.

L4 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:67768 CAPLUS
DOCUMENT NUMBER: 128:166045
TITLE: Mice are protected from **Helicobacter** pylori infection by nasal **immunization** with **attenuated Salmonella**

typhimurium phoPc expressing **urease** A and B subunits

AUTHOR(S): Corthesy-Theulaz, Irene E.; Hopkins, Sally; Bachmann, Daniel; Saldinger, Pierre F.; Porta, Nadine; Haas, Rainer; Zheng-Xin, Yan; Meyer, Thomas; Bouzourene, Hanifa; Blum, Andre L.; Kraehenbuhl, Jean-Pierre

CORPORATE SOURCE: Division of Gastroenterology, Department of Internal Medicine CHUV, Lausanne, CH-1011, Switz.

SOURCE: Infect. Immun. (1998), 66(2), 581-586
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Live **Salmonella** typhimurium phoPc bacteria were tested as mucosal **vaccine** vectors to deliver **Helicobacter** pylori antigens. The genes encoding the A and B subunits of H. pylori **urease** were introduced into S. typhimurium phoPc and expressed under the control of a constitutive tac promoter (tac-ureAB) or a two-phase T7 expression system (cT7-ureAB). Both **recombinant Salmonella** strains expressed the two **urease** subunits in vitro and were used to nasally **immunize** BALB/c mice. The plasmid carrying cT7-ureAB was stably inherited by bacteria growing or persisting in the spleen, lungs, mesenteric or cervical lymph nodes, and Peyer's patches of **immunized** mice, while the plasmid carrying tac-ureAB was rapidly lost. Spleen and Peyer's patch CD4+ lymphocytes from mice **immunized** with S. typhimurium phoPc cT7-ureAB proliferated in vitro in response to **urease**, whereas cells from mice given S. typhimurium phoPc alone did not. Splenic CD4+ cells from mice **immunized** with phoPc cT7-ureAB secreted gamma interferon and interleukin 10, while Peyer's patch CD4+ cells did not secrete either cytokine. Specific H. pylori anti-**urease** IgG1 and IgG2a antibodies were detected following **immunization**, confirming that both Th1- and Th2-type immune responses were generated by the live **vaccine**. Sixty percent of the mice (9 of 15) **immunized** with S. typhimurium phoPc cT7-ureAB were resistant to infection by H. pylori, while all mice **immunized** with phoPc tac-ureAB (15 of 15) or phoPc (15 of 15) were infected. The data demonstrate that H. pylori **urease** delivered nasally by using a **vaccine** strain of S. typhimurium can trigger Th1- and Th2-type responses and induce protective immunity against **Helicobacter** infection.

L4 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:530603 CAPLUS

DOCUMENT NUMBER: 127:204061

TITLE: **Vaccine** development against **Helicobacter** pylori infections
AUTHOR(S): Haas, Rainer; Meyer, Thomas F.
CORPORATE SOURCE: Max-Planck-Institut fur Biologie, Abteilung Infektionsbiologie, Tubingen, D-72076, Germany
SOURCE: Biologicals (1997), 25(2), 175-177
CODEN: BILSEC; ISSN: 1045-1056
PUBLISHER: Academic
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 13 refs. Topics discussed include: animal models for **vaccine** development, identification of H. pylori antigens providing protection against **Helicobacter** infection, prophylactic and therapeutic **immunization** strategies, the basis of protective immunity, new strategies to identify further efficient **vaccine** candidates, and use of **attenuated Salmonella** strains as live **vaccine** carriers for H. pylori antigens.

L4 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:366380 CAPLUS
DOCUMENT NUMBER: 126:329512
TITLE: Live **vaccines** against Gram-negative **pathogens**, expressing heterologous O-antigens
INVENTOR(S): Favre, Didier; Cryz, Stanley J.; Viret, Jean-francois
PATENT ASSIGNEE(S): Swiss Serum and Vaccine Institute Berne, Switz.; Favre, Didier; Cryz, Stanley, J.; Viret, Jean-Francois
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714782	A1	19970424	WO 1996-EP4334	19961004
W: AU, CA, CU, JP, KR, MX, SG, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2232563	AA	19970424	CA 1996-2232563	19961004
AU 9672859	A1	19970507	AU 1996-72859	19961004
EP 854914	A1	19980729	EP 1996-934548	19961004
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000506368	T2	20000530	JP 1997-515470	19961004

PRIORITY APPLN. INFO.: EP 1995-116208 19951013
WO 1996-EP4334 19961004

AB The present invention relates to live **attenuated** Gram-neg. **vaccine** carrier strains which are useful for expression and delivery of heterologous O-antigens (O-PS) from Gram-neg. **pathogens**. Said strains are deficient in the expression of homologous O-PS due to a defined genetic modification, preferably a deletion, and, thus, capable of efficiently expressing a desired heterologous O-PS in such a way that it is covalently coupled either to homologous or heterologous LPS core lipid A. The present invention furthermore relates to live **vaccine** carrier strains contg. a heterologous gene or a set of heterologous genes encoding O-PS. Preferably, said strains addnl. contain genes necessary for the synthesis of complete smooth heterologous LPS. The present invention also relates to live **vaccines** comprising said strains, preferably for **immunization** against Gram-neg. enteric **pathogens**. An rfbAB deletion mutant of Vibrio cholerae CVD103-HgR, called CH19, was prepd. The rfb/rfc locus of Shigella sonnei was integrated into the genome of CH19, producing live **vaccine** strain CH22. **Immunization** of mice with CH22 induced high titers of anti-S. sonnei LPS antibodies but no anti-V. cholerae LPS antibodies.

L4 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:756534 CAPLUS
DOCUMENT NUMBER: 126:17798
TITLE: Method for introducing and expressing genes in animal cells
INVENTOR(S): Powell, Robert J.; Lewis, George K.; Hone, David M.
PATENT ASSIGNEE(S): University of Maryland At Baltimore, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9634631	A1	19961107	WO 1996-US5326	19960424
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5877159	A	19990302	US 1995-433790	19950503
CA 2219994	AA	19961107	CA 1996-2219994	19960424
AU 9655527	A1	19961121	AU 1996-55527	19960424
AU 706104	B2	19990610		

Searcher : Shears 308-4994

EP 827410 A1 19980311 EP 1996-912850 19960424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 11505219 T2 19990518 JP 1996-533329 19960424
PRIORITY APPLN. INFO.: US 1995-433790 19950503
WO 1996-US5326 19960424

AB A method for introducing an expressing genes in animal cells is disclosed comprising infecting said animal cells with live invasive bacteria, wherein said bacteria contain a eukaryotic expression cassette encoding said gene. The gene may encode, e.g., **vaccine** antigen, a therapeutic agent, and immunoregulatory agent or an anti-sense RNA or a catalytic RNA. Prepd. were **attenuated** Shigella flexneri-infected HeLa cell, human peripheral blood-derived mononuclear cells, and animal cell line CCL-6, CCL-34 and HTB-37.

L4 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:740354 CAPLUS
DOCUMENT NUMBER: 126:6446
TITLE: Protective **Helicobacter** antigens
INVENTOR(S): Doidge, Christopher Vincent; Lee, Adrian; Radcliff, Fiona Jane; Hocking, Dianna Margaret; Webb, Elizabeth Ann
PATENT ASSIGNEE(S): Csl Ltd., Australia
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633220	A1	19961024	WO 1996-AU225	19960419
W: AU, CA, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2217496	AA	19961024	CA 1996-2217496	19960419
AU 9652621	A1	19961107	AU 1996-52621	19960419
AU 693679	B2	19980702		
EP 821698	A1	19980204	EP 1996-908930	19960419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11504206	T2	19990420	JP 1996-531353	19960419
PRIORITY APPLN. INFO.:			AU 1995-2575	19950421
			AU 1995-3931	19950703
			AU 1996-7565	19960116
			WO 1996-AU225	19960419

AB Protective **Helicobacter** antigens, esp. H. pylori antigens,

and the use of these antigens as **vaccines** for the treatment or prevention of gastroduodenal disease assocd. with H. pylori infection. Mol. cloning of H. pylori antigens or proteins was performed, and **recombinant** H. pylori antigens (i.e. 13, 17, 19, 29, 36 and 50 kDa) were cloned. subcloned, expressed, purified, and tested in mouse model.

L4 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:647040 CAPLUS
DOCUMENT NUMBER: 125:295804
TITLE: Cloning, sequencing, expression, purification and preliminary characterization of a type II dehydroquinase from **Helicobacter** pylori
AUTHOR(S): Bottomley, Joanna R.; Clayton, Christopher L.; Chalk, Peter A.; Kleanthous, Colin
CORPORATE SOURCE: Sch. Biological Sci., Univ. East Anglia, Norwich, NR4 7TJ, UK
SOURCE: Biochem. J. (1996), 319(2), 559-565
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A heat-stable dehydroquinase was purified to near homogeneity from a plate-grown suspension of the Gram-neg. stomach **pathogen** **Helicobacter** pylori, and shown from both its subunit and native mol. masses to be a member of the type II family of dehydroquinases. This was confirmed by N-terminal amino acid sequence data. The gene encoding this activity was isolated following initial identification, by random sequencing of the H. pylori genome, of a 96 bp fragment, the translated sequence of which showed strong identity to a C-terminal region of other type II enzymes. Southern blot anal. of a cosmid library identified several potential clones, one of which complemented an Escherichia coli aroD point mutant strain deficient in host dehydroquinase. The gene encoding the H. pylori type II dehydroquinase (designated aroQ) was sequenced. The translated sequence was identical to the N-terminal sequence obtained directly from the purified protein, and showed strong identity to other members of the type II family of dehydroquinases. The enzyme was readily expressed in E. coli from a plasmid construct from which several milligrams of protein could be isolated, and the mol. mass of the protein was confirmed by electrospray MS. The aroQ gene in H. pylori may function in the central biosynthetic shikimate pathway of this bacterium, thus opening the way for the construction of **attenuated** strains as potential **vaccines** as well as offering a new target for selective enzyme inhibition.

L4 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:566987 CAPLUS

DOCUMENT NUMBER: 123:7704
TITLE: Severe and prolonged inflammatory response to localized cowpox virus infection in footpads of C5-deficient mice: investigation of the role of host complement in poxvirus pathogenesis
AUTHOR(S): Miller, Cathie G.; Justus, David E.; Jayaraman, Sundararajan; Kotwal, Girish J.
CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. Louisville School Medicine, Louisville, KY, 40292, USA
SOURCE: Cell. Immunol. (1995), 162(2), 326-32
CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Poxviruses are a large, complex group of highly successful **pathogens** that cause disease in humans and other animals. They encode several proteins postulated to be involved in the evasion of host immunity and therefore serve as excellent models for understanding virus-host interaction during the early stages of viral infection. **Vaccinia** virus, the best characterized member of the poxviridae family, encodes a 35-kDa major **secretory polypeptide** termed **vaccinia** virus complement control protein (VCP), which is structurally related to the family of human and mouse complement control proteins. Members of the family of complement control proteins have been shown to inhibit complement mediated opsonization of bacteria and induction of inflammatory and phagocytic responses in vitro. Insertional inactivation of the VCP gene results in **attenuation** of viral virulence in vivo. The role of host complement in the inflammatory response to poxvirus infection has not been systematically investigated. Prior to detg. the role of VCP on inflammatory responses in vivo, the authors decided to investigate the role of host complement in the progression of viral infection. They compared the effects of injection of cowpox virus, primarily a rodent virus, into footpads of congenic mice strains B10.D2/nSnJ (C5-sufficient) and B10.D2/oSnJ (C5-deficient). The effects of the injection were monitored macroscopically by measuring the specific swelling response immediately following primary injection and subsequently after reinjection and by histol. examn. of the stained sections of the foot-pads. Evidently there is a variation in the primary response in the two different mouse strains to cowpox virus infection. The specific swelling response obsd. in measurements from the footpads of the B10.D2/oSnJ mice was greater, persisted for a longer duration, and was accompanied by severe ulceration, edema, induration, and hemorrhaging. Reinjection of the footpads after a 3-mo period, during which time the swelling had subsided and the footpad had fully recovered to its original size and appearance, showed no differences between the two strains. Apparently, the host complement plays a role during the initial response to poxvirus infection.

L4 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:73285 CAPLUS
DOCUMENT NUMBER: 120:73285
TITLE: Nutrient phospholipids for pathogenic bacteria
INVENTOR(S): Krivan, Howard C.
PATENT ASSIGNEE(S): Microcarb Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9322423	A1	19931111	WO 1993-US4053	19930429
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 1992-875510	19920429

AB Bacterial, esp. pathogenic bacteria, are grown on lipids, phospholipids, phosphatidylserine, or mucus, egg or milk fractions or subfractions. The pathogenic bacteria are selected from **Salmonella**, Yersinia, Shigella, Campylobacter, **Helicobacter**, Pseudomonas, Streptococcus, Staphylococcus, E. coli, Haemophilus, Mycobacterium, Proteus, Klebsiella, Neisseria, Branhamella, Bacteroides, Listeria, Enterococci, Vibrio, Yersinia, Bordetella, Clostridium, Treponema, and Mycoplasma. The present invention are useful for the selection of mutant strains which cannot grow in animals and use of the mutants as host cells for gene expression. In addn., The invention is also useful for the prepn. of antigen or **vaccines**.

L4 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:145422 CAPLUS
DOCUMENT NUMBER: 118:145422
TITLE: Antigen selection and presentation to protect against transmissible gatroenteritis coronavirus
AUTHOR(S): Enjuanes, Luis; Sune, Carlos; Gebauer, Fatima; Smerdou, Cristian; Camacho, Ana; Anton, Ines M.; Gonzalez, Silvia; Talamillo, Ana; Mendez, Ana; et al.
CORPORATE SOURCE: Cent. Nac. Biotecnol., Univ. Auton., Madrid, Spain
SOURCE: Vet. Microbiol. (1992), 33(1-4), 249-62
CODEN: VMICDQ; ISSN: 0378-1135
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antigenic structure of the S glycoprotein of transmissible gastroenteritis virus (TGEV) and porcine respiratory coronavirus (PRCV) was detd. and correlated with the phys. structure. Four antigenic sites were defined (A, B, C, and D). The sites involved in the neutralization of TGEV are: A, D, and B, sites A and D being antigenically dominant for TGEV neutralization in vitro. These 2 sites have specific properties of interest: site A is highly conserved and is present in coronaviruses of 3 animal species, and site D can be represented by synthetic peptides. Both sites might be relevant in protection in vivo. PRCV does not have sites B and C, due to a genomic deletion. Complex antigenic sites, i.e., conformation and glycosylation dependent sites, have been represented by simple **mimotopes** selected from a library expressing **recombinant** peptides with random sequences, or by anti-idiotypic internal image monoclonal antibodies. An epidemiol. tree relating the TGEVs and PRCVs has been proposed. The estd. mutation fixation rate of 7 .times. 10-4 substitutions per nucleotide and year indicates that TGEV related coronaviruses show similar variability to other RNA viruses. In order to induce secretory immunity, different segments of the S gene were expressed using a virulent forms of **Salmonella** typhimurium and adenovirus. These vectors, with a tropism for Peyer's patches may be ideal candidates in protection against TGEV.

(FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS, TOXLIT, TOXLINE, PHIC, PHIN' ENTERED AT 16:10:44 ON 14 JUN 2000)

L5 103 S L4
L6 73 DUP REM L5 (30 DUPLICATES REMOVED)
L7 13 S L6 AND (LIVE OR LIVING)

L7 ANSWER 1 OF 13 MEDLINE
ACCESSION NUMBER: 2000196979 MEDLINE
DOCUMENT NUMBER: 20196979
TITLE: The impact of new technologies on **vaccines**.
AUTHOR: Talwar G P; Diwan M; Razvi F; Malhotra R
CORPORATE SOURCE: Talwar Research Foundation, New Delhi, India.
SOURCE: NATIONAL MEDICAL JOURNAL OF INDIA, (1999 Nov-Dec) 12 (6) 274-80. Ref: 75
Journal code: BNT. ISSN: 0970-258X.
PUB. COUNTRY: India
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
ENTRY MONTH: 200006
ENTRY WEEK: 20000603
AB Vast changes are taking place in **vaccinology** consequent to the introduction of new technologies. Amongst the **vaccines** included in the Expanded Programme of **Immunization** (EPI),

the pertussis **vaccine** has been replaced by acellular purified fractions devoid of side-effects. Non-pathogenic but immunogenic mutants of tetanus and diptheria toxins are likely to replace the toxoids. An effective **vaccine** against hepatitis B prepared by **recombinant** technology is in large-scale use. Conjugated **vaccines** against Haemophilus influenzae b, S. pneumococcus and meningococcus are now available, as also **vaccines** against mumps, rubella and measles. Combination **vaccines** have been devised to limit the number of injections. **Vaccine** delivery systems have been developed to deliver multiple doses of the **vaccine** at a single contact point. A genetically-engineered oral **vaccine** for typhoid imparts better and longer duration of immunity. Oral **vaccines** for cholera and other enteric infections are under clinical trials. The nose as a route for **immunization** is showing promise for mucosal immunity and for anti-inflammatory experimental **vaccines** against multiple sclerosis and insulin-dependent diabetes mellitus. The range of **vaccines** has expanded to include **pathogens** resident in the body such as **Helicobacter** pylori (duodenal ulcer), S. mutans (dental caries), and human papilloma virus (carcinoma of the cervix). An important progress is the recognition that DNA alone can constitute the **vaccines**, inducing both humoral and cell-mediated immune responses. A large number of DNA **vaccines** have been made and shown interesting results in experimental animals. **Live recombinant vaccines** against rabies and rinderpest have proven to be highly effective for controlling these infections in the field, and those for AIDS are under clinical trial. Potent adjuvants have added to the efficacy of the **vaccines**. New technologies have emerged to 'humanize' mouse monoclonals by genetic engineering and express these efficiently in plants. These **recombinant** antibodies are opening out an era of highly specific and safe therapeutic interventions. Human **recombinant** antibodies would be invaluable for treating patients with terminal tetanus and rabies. Antibodies are already in use for treatment of cancer, rheumatoid arthritis and allergies. An advantage of preformed antibodies directed at a defined target and given in adequate amounts is the certainty of efficacy in every recipient, in contrast to **vaccines**, where the quality and quantum of immune response varies from individual to individual.

L7 ANSWER 2 OF 13 MEDLINE
ACCESSION NUMBER: 1999451179 MEDLINE
DOCUMENT NUMBER: 99451179
TITLE: Safety and immunogenicity of phoP/phoQ-deleted **Salmonella** typhi expressing **Helicobacter** pylori **urease** in adult volunteers.

Searcher : Shears 308-4994

AUTHOR: DiPetrillo M D; Tibbetts T; Kleanthous H; Killeen K P; Hohmann E L
CORPORATE SOURCE: Infectious Disease Division, Department of Medicine, Massachusetts General Hospital, Boston 02114, USA.
CONTRACT NUMBER: R29AI40672 (NIAID)
M01 RR01066-21 (NCRR)
SOURCE: VACCINE, (1999 Oct 14) 18 (5-6) 449-59.
Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY WEEK: 20000303
AB **Salmonella** typhi Ty800, deleted for the **Salmonella** phoP/phoQ virulence regulon has been shown to be a safe and immunogenic single dose oral typhoid fever **vaccine** in volunteers. This promising **vaccine** strain was modified to constitutively express a heterologous protein of Gram negative bacterial origin, **Helicobacter** pylori **urease** subunits A and B, yielding S. typhi strain Ty1033. Seven volunteers received single oral doses of > or = 10(10) colony forming units of Ty1033; an eighth volunteer received two doses 3 months apart. Side effects were similar to those observed previously in volunteers who received the unmodified vector Ty800. All volunteers had strong mucosal immune responses to **vaccination** as measured by increases in IgA-secreting cells in peripheral blood directed against S. typhi antigens. Seven of eight volunteers had convincing seroconversion as measured by increases in serum IgG directed against S. typhi flagella and lipopolysaccharide antigens by ELISA. No volunteer had detectable mucosal or humoral immune responses to the **urease** antigen after **immunization** with single doses of Ty1033. A subset of three volunteers received an oral booster **vaccination** consisting of **recombinant** purified H. pylori **urease** A/B and E. coli heat labile toxin adjuvant 15 days after **immunization** with Ty1033. None of three had detectable humoral or mucosal immune responses to **urease**. Expression of a stable immunogenic protein in an appropriately **attenuated** S. typhi vector did not engender detectable mucosal or systemic antibody responses; additional work will be needed to define variables important for immunogenicity of heterologous antigens carried by **live** S. typhi vectors in humans.

L7 ANSWER 3 OF 13 MEDLINE
ACCESSION NUMBER: 1999210725 MEDLINE
DOCUMENT NUMBER: 99210725
TITLE: The **attenuated Salmonella** **vaccine** approach for the control of

Helicobacter pylori-related diseases.

AUTHOR: Gomez-Duarte O G; Bumann D; Meyer T F
CORPORATE SOURCE: Abteilung Infektionsbiologie, Max-Planck-Institut fur Biologie, Tubingen, Germany.
SOURCE: VACCINE, (1999 Mar 26) 17 (13-14) 1667-73. Ref: 81
Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY WEEK: 19990705

AB The Gram-negative bacterium **Helicobacter** pylori is a widespread human **pathogen** that colonizes the gastric mucosa and is associated with gastro-intestinal illnesses such as gastritis, peptic ulcer, gastric lymphoma and gastric cancer. Current pharmacological therapies are becoming less reliable for the control of H. pylori due to the elevated costs and to the increasing number of antibiotic resistant strains. New **vaccination** strategies utilizing H. pylori antigens combined with adjuvants or delivery of antigens by **attenuated Salmonella** strains have been successful in protecting mice against H. pylori infections. Oral **immunization** with single doses of **urease**-expressing **Salmonella vaccine** strains elicits mucosal and systemic antibody responses and fully protects different mouse strains against challenge infections with H. pylori. The high efficacy in the mouse model, combined with remarkable immunogenicity, safety and low-cost production, makes **attenuated live recombinant** **Salmonella** promising **vaccine** candidates for the control of H. pylori-related diseases in humans.

L7 ANSWER 4 OF 13 MEDLINE
ACCESSION NUMBER: 1998152200 MEDLINE
DOCUMENT NUMBER: 98152200
TITLE: Protection of mice against gastric colonization by **Helicobacter** pylori by single oral dose **immunization** with **attenuated** **Salmonella** typhimurium producing **urease** subunits A and B.
AUTHOR: Gomez-Duarte O G; Lucas B; Yan Z X; Panthel K; Haas R; Meyer T F
CORPORATE SOURCE: Max-Planck-Institut fur Biologie, Abteilung Infektionsbiologie, Tubingen, Germany.
SOURCE: VACCINE, (1998 Mar) 16 (5) 460-71.
Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY WEEK: 19980603

AB **Helicobacter** pylori is a Gram-negative bacterial **pathogen** associated with gastritis, peptic ulceration, and gastric carcinoma. The bacteria express a strong **urease** activity which is known to be essential for colonization of gnotobiotic pigs and nude mice. UreA and UreB, two structural subunits of the active enzyme, were expressed in the **attenuated Salmonella** typhimurium **live vaccine** SL3261 strain. Evaluation of protection against H. pylori was performed in Balb/c mice by oral **immunization** with a single dose of the **vaccine** strain. Five weeks after **immunization**, mice were challenged orally three times with a mouse-adapted H. pylori wild type strain and, six weeks later, mice were sacrificed to determine H. pylori infection by detection of **urease** activity from the antral region of the mouse stomachs. In several independent experiments, we observed 100% infection with H. pylori in the non-**immunized** mice and no infection (100% protection) in the mice **immunized** with S. typhimurium expressing **recombinant** UreA and UreB. Specific humoral and mucosal antibody responses against UreA and UreB were observed in mice **immunized** as indicated by western blots and ELISA assays. These data shows that oral **immunization** of mice with **urease** subunits delivered by an **attenuated Salmonella** strain induced a specific immune response and protected mice against H. pylori colonization. Single oral dose **immunization** with UreA and UreB delivered by a **live Salmonella vaccine** vector appears to be an attractive candidate for human **vaccination** against H. pylori infection. In addition, this model will aid to elucidate the effective protection mechanisms against H. pylori in the gastric mucosa.

L7 ANSWER 5 OF 13 MEDLINE
ACCESSION NUMBER: 1998114357 MEDLINE
DOCUMENT NUMBER: 98114357
TITLE: Mice are protected from **Helicobacter** pylori infection by nasal **immunization** with **attenuated Salmonella** typhimurium phoPc expressing **urease** A and B subunits.
AUTHOR: Corthesy-Theulaz I E; Hopkins S; Bachmann D; Saldinger P F; Porta N; Haas R; Zheng-Xin Y; Meyer T; Bouzour`ene H; Blum A L; Kraehenbuhl J P
CORPORATE SOURCE: Department of Internal Medicine CHUV, and Institute of Pathology, Lausanne University, Switzerland.. Irene.CorthesyTheulaz@ipharm.unil.ch

SOURCE: INFECTION AND IMMUNITY, (1998 Feb) 66 (2) 581-6.
Journal code: GO7. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199804
ENTRY WEEK: 19980402

AB **Live Salmonella** typhimurium phoPc bacteria were tested as mucosal **vaccine** vectors to deliver **Helicobacter** pylori antigens. The genes encoding the A and B subunits of H. pylori **urease** were introduced into S. typhimurium phoPc and expressed under the control of a constitutive tac promoter (tac-ureAB) or a two-phase T7 expression system (cT7-ureAB). Both **recombinant Salmonella** strains expressed the two **urease** subunits in vitro and were used to nasally **immunize** BALB/c mice. The plasmid carrying cT7-ureAB was stably inherited by bacteria growing or persisting in the spleen, lungs, mesenteric or cervical lymph nodes, and Peyer's patches of **immunized** mice, while the plasmid carrying tac-ureAB was rapidly lost. Spleen and Peyer's patch CD4+ lymphocytes from mice **immunized** with S. typhimurium phopc cT7-ureAB proliferated in vitro in response to **urease**, whereas cells from mice given S. typhimurium phoPc alone did not. Splenic CD4+ cells from mice **immunized** with phoPc cT7-ureAB secreted gamma interferon and interleukin 10, while Peyer's patch CD4+ cells did not secrete either cytokine. Specific H. pylori anti-**urease** immunoglobulin G1 (IgG1) and IgG2A antibodies were detected following **immunization**, confirming that both Th1- and Th2-type immune responses were generated by the **live vaccine**. Sixty percent of the mice (9 of 15) **immunized** with S. typhimurium phoPc cT7-ureAB were found to be resistant to infection by H. pylori, while all mice **immunized** with phoPc tac-ureAB (15 of 15) or phoPc (15 of 15) were infected. Our data demonstrate that H. pylori **urease** delivered nasally by using a **vaccine** strain of S. typhimurium can trigger Th1- and Th2-type responses and induce protective immunity against **Helicobacter** infection.

L7 ANSWER 6 OF 13 MEDLINE

ACCESSION NUMBER: 1998020884 MEDLINE
DOCUMENT NUMBER: 98020884

TITLE: Bacterial ghosts as multifunctional **vaccine** particles.

AUTHOR: Szostak M P; Mader H; Truppe M; Kamal M; Eko F O; Huter V; Marchart J; Jechlinger W; Haidinger W; Brand E; Denner E; Resch S; Dehlin E; Katinger A; Kuen B; Haslberger A; Hensel A; Lubitz W
CORPORATE SOURCE: Institute of Microbiology and Genetics, University of

Vienna, Austria.
SOURCE: BEHRING INSTITUTE MITTEILUNGEN, (1997 Feb) (98) 191-6.
Journal code: 9KI. ISSN: 0301-0457.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY WEEK: 19980104

AB Expression of cloned PhiX174 gene E in Gram-negative bacteria results in lysis of the bacteria by formation of an E-specific transmembrane tunnel structure built through the cell envelope complex. Bacterial ghosts have been produced from a variety of bacteria including Escherichia coli. **Salmonella** typhimurium, **Salmonella** enteritidis, Vibrio cholerae, Klebsiella pneumoniae, Actinobacillus pleuropneumoniae, Haemophilus influenzae, Pasteurella haemolytica, Pasteurella multocida, and **Helicobacter** pylori. Such ghosts are used as non-**living** candidate **vaccines** and represent an alternative to heat or chemically inactivated bacteria. In **recombinant** ghosts, foreign proteins can be inserted into the inner membrane prior to E-mediated lysis via specific N-, or C-, or N- and C-terminal anchor sequences. The export of proteins into the periplasmic space or the expression of **recombinant** S-layer proteins vastly extents the capacity of ghosts or **recombinant** ghosts as carriers of foreign epitopes or proteins. Oral, aerogenic or parenteral applications of (**recombinant**) ghosts in experimental animals induced specific humoral and cellular immune responses against bacterial and target components including protective mucosal immunity. The most relevant advantage of ghosts and **recombinant** bacterial ghosts as immunogens is that no inactivation procedures that denature relevant immunogenic determinants are employed in the production of ghosts used as **vaccines** or as carriers of relevant antigens. The inserted target antigens into the inner membrane or into S-layer proteins are not limited in size.

L7 ANSWER 7 OF 13 MEDLINE

ACCESSION NUMBER: 97118683 MEDLINE
DOCUMENT NUMBER: 97118683
TITLE: **Vaccination** against **Helicobacter** pylori.
AUTHOR: Lee A
CORPORATE SOURCE: School of Microbiology and Immunology, University of New South Wales, Sydney, Australia.
SOURCE: JOURNAL OF GASTROENTEROLOGY, (1996 Nov) 31 Suppl 9 69-74. Ref: 50
Journal code: BWP. ISSN: 0944-1174.
Searcher : Shears 308-4994

PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY WEEK: 19970602

AB The initial steps have been taken towards the development of a **vaccine** against the human gastroduodenal **pathogen**, **Helicobacter** pylori. Proof of principle was achieved when mice were protected against challenge with **living** **Helicobacter** felis, a close relative of the human **pathogen**, following oral **immunization** with H. felis sonicate and the mucosal adjuvant, cholera toxin. Similar results with H. pylori antigen have allowed development of possible human **vaccines**. **Recombinant urease** protein has been proposed as a major **vaccine** candidate, together with the heat-labile toxin of Escherichia coli as the adjuvant. Probably the most significant finding in the early **vaccine** studies was that **immunization** of already infected mice resulted in a cure of **Helicobacter** infection. The possibility of a therapeutic **vaccine** makes commercial development more attractive, as large populations could be **immunized** without the potential for development of drug-resistant strains that currently restricts widespread antibiotic use. For advanced societies with powerful economies yet a high prevalence of H. pylori, such as Japan, **vaccine** development should become a high national health priority.

L7 ANSWER 8 OF 13 MEDLINE
ACCESSION NUMBER: 95317474 MEDLINE
DOCUMENT NUMBER: 95317474
TITLE: The history of **live** bacterial **vaccines**.
AUTHOR: Lindberg A A
CORPORATE SOURCE: Lederle-Praxis Biologicals, Wayne, NJ, USA..
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1995) 84 211-9.
Journal code: E7V. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
Historical
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510

AB Recent developments have made it possible to construct non-reverting **live** bacterial **vaccine** candidates with defined deletions of two or more genes. Such **vaccines** have proven

safe and immunogenic in human volunteers. Since the virulent parent strains are only pathogenic to man (S. typhi, S. flexneri, and V. cholerae), they pose no threat to the environment. Besides holding promise as efficacious **vaccines** for protection against typhoid fever, bacillary dysentery and cholera, the **attenuated** strains are well suited as vectors for delivery of heterologous antigenic epitopes from micro-organisms such as **Helicobacter** pylori, Neisseira gonorrhoeae, rotavirus, HIV and many others. Instead of using a virulent parent bacterium as the starting organism for making a vector, attempts have recently been made to employ non-pathogenic bacteria of the normal human flora, such as Streptococcus gordonii for delivery of foreign antigens. At present, the feasibility of this approach for human beings remains to be proven.

L7 ANSWER 9 OF 13 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:303516 BIOSIS
DOCUMENT NUMBER: PREV199800303516
TITLE: **Recombinant** cholera toxin B subunit is not an effective mucosal adjuvant for oral **immunization** of mice against **Helicobacter** felis.
AUTHOR(S): Blanchard, T. G.; Lycke, N.; Czinn, S. J.; Nedrud, J. G. (1)
CORPORATE SOURCE: (1) Pathol. Dep., Biomed. Res. Build., Case Western Reserve Univ., 10 900 Euclid Ave., Cleveland, OH 44106-4943 USA
SOURCE: Immunology, (May, 1998) Vol. 94, No. 1, pp. 22-27. ISSN: 0019-2805.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Cholera toxin is a potent oral mucosal adjuvant for enteric **immunization**. Several studies suggest that commercial cholera toxin B subunit (cCTB; purified from holotoxin) may be an effective non-toxic alternative for oral **immunization**. The present study was performed, using an infectious disease model, to determine if the oral mucosal adjuvanticity of CTB is dependent on contaminating holotoxin. Mice were orally **immunized** with **Helicobacter** felis sonicate and either cholera holotoxin, cCTB or **recombinant** cholera toxin B subunit (rCTB). Serum immunoglobulin G (IgG) and intestinal immunoglobulin A (IgA) antibody responses were determined and the mice were challenged with **live** H. felis to determine the degree of protective immunity induced. All orally **immunized** mice responded with serum IgG antibody titres regardless of the adjuvant used. However, only mice **immunized** with either holotoxin or the cCTB responded with an intestinal mucosal IgA response. Consistent with the production of mucosal antibodies, mice **immunized** with either holotoxin or cCTB as adjuvants were protected from challenge

while mice receiving H. felis sonicate and rCTB all became infected. cCTB induced the accumulation of cAMP in mouse thymocytes at a level equal to 0.1% of that induced by holotoxin, whereas rCTB was devoid of any activity. These results-indicate that CTB possesses no intrinsic mucosal adjuvant activity when administered orally. Therefore, when used as an oral adjuvant, CTB should also include small, non-toxic doses of cholera toxin.

L7 ANSWER 10 OF 13 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1993:453976 BIOSIS
DOCUMENT NUMBER: PREV199396098876
TITLE: Cloning and sequencing of the glucosyl transferase-encoding gene from converting bacteriophage X (SFX) of Shigella flexneri.
AUTHOR(S): Verma, Naresh K. (1); Verma, Donna J.; Huan, Pham Thi; Lindberg, Alf A.
CORPORATE SOURCE: (1) HHMI, Dep. Microbiology Immunology, Beckman Cent., B239, Stanford Univ. Sch. Med., Stanford, CA 94305 USA
SOURCE: Gene (Amsterdam), (1993) Vol. 129, No. 1, pp. 99-101. ISSN: 0378-1119.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Shigella flexneri type Y strains (-;3,4) are converted to type X (-;7,8) by bacteriophage X (SFX) that causes glucosylation of the O-antigenic polysaccharide chain. The gene (gtr) encoding glucosyl transferase from bacteriophage X has been cloned and sequenced. The protein encoded by gtr consists of 416 amino acids with a M-r of 47 369. The cloned gtr product was able to convert a S. flexneri strain type Y (SFL 124, a **live attenuated** candidate **vaccine** strain) to type X. The importance of the hybrid strain in **vaccine** development is discussed.

L7 ANSWER 11 OF 13 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998139461 EMBASE
TITLE: Sequencing microbial genomes - What will it do for microbiology?.
AUTHOR: Jenks P.J.
CORPORATE SOURCE: P.J. Jenks, Unite Pathogenie Bacterienne, Institut Pasteur, 25-28 Rue de Dr Roux, 75724 Paris, France
SOURCE: Journal of Medical Microbiology, (1998) 47/5 (375-382).
Refs: 43
ISSN: 0022-2615 CODEN: JMMIAV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
Searcher : Shears 308-4994

LANGUAGE: English
SUMMARY LANGUAGE: English
AB In 1995, Haemophilus influenzae became the first free-**living** organism to have its entire genome sequence published. Since then, many similar projects have been started and, by the millennium, the genomes of a significant number of important human **pathogens** will have been sequenced. During this period of increasing access to microbial sequence data, parallel advances have occurred in techniques that allow the large-scale study of the entire genetic complement of micro-organisms. In the near future, these approaches will enable researchers to unravel further the complexity of microbial pathogenesis and identify new virulence determinants. Many of these will be suitable targets for development as diagnostic reagents, antimicrobial agents and **vaccine** candidates. Although it is difficult to predict the full impact that this almost overwhelming volume of information will have on the practice of microbiology, it is clear that it will result ultimately in new ways of diagnosing and combating infectious diseases.

L7 ANSWER 12 OF 13 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97212801 EMBASE
DOCUMENT NUMBER: 1997212801
TITLE: Mucosal **immunisation** for enteric diseases: Current practice and future prospects.
AUTHOR: Sabbaj S.; Kiyono H.; McGhee J.R.
CORPORATE SOURCE: Dr. S. Sabbaj, Department of Microbiology, University of Alabama, 845 19th Street South, Birmingham, AL 35294-2170, United States
SOURCE: BioDrugs, (1997) 7/2 (134-157).
Refs: 151
ISSN: 1173-8804 CODEN: BIDRF4
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Oral delivery of **vaccines** results in these being taken up by specialised microfold epithelial cells covering Peyer's patches of the gastrointestinal tract, therefore stimulating regulatory T cells and surface IgA positive (sIgA+) B cells. T helper cells can be divided into 2 subsets, type 1 (T(H)1) and type 2 (T(H)2), according to their function and the cytokines they secrete. T(H)1 cytokines such as interleukin (IL)-2, interferon-.gamma. and tumour necrosis factor-.beta. (TNF.beta.) elicit activation of T cells and macrophages, whereas T(H)2 cytokines such as IL-4, IL-5, IL-6 and IL-10 favour mucosal and parenteral B cell responses. Therefore,

T(H)2-type T cells are of particular interest for mucosal responses, since they help in the differentiation of sIgA+ B cells into IgA-producing plasma cells. As a result, one can take advantage of the fact that different forms of antigen delivery systems generally influence the outcome of an immune response, and use these that best induce mucosal responses. An example of this would be orally administered **live attenuated Salmonella** versus the oral administration of cholera toxin. The first induces a dominant T(H)1-type response, and the second a T(H)2-type response. Thus these 2 delivery systems can be exploited in order to elicit the desired immune response depending on the protective response required. Alternatively, encapsulating antigens into polyglycolide microspheres or liposomes, or incorporating them into immune-stimulating complexes, has facilitated the delivery of antigens which otherwise do not result in an immune response when given orally. Much progress is being made in the construction of **attenuated** viral and bacterial vectors for the delivery of antigen to mucosal sites. For example, poliovirus has been used as a vector to deliver both rotavirus and HIV antigens. Bacterial vectors and **attenuated** mutant bacteria for use in **vaccines** have also been extensively researched. Examples of these include **Salmonella** typhi mutants. Vibrio cholera, Shigella species, **Helicobacter** pylori and Campylobacter jejuni. In addition, new approaches are being developed to induce responses at mucosal surfaces such as the gastrointestinal, respiratory and genitourinary tracts. These include the use of adjuvants that stimulate mucosal responses such as cholera toxin and Escherichia coli heat labile toxin, as well as the coexpression of cytokine genes with antigenic proteins on **live** vectors to drive the immune response so that mucosal responses are favoured. Furthermore, nucleic acid **vaccines** and the potential use of transgenic plants are new technologies that are contributing to our ability to induce responses at mucosal surfaces.

L7 ANSWER 13 OF 13 COPYRIGHT 2000 PJB

ACCESSION NUMBER: 1998:16790 PHIN
DOCUMENT NUMBER: S00594908
DATA ENTRY DATE: 18 Sep 1998
TITLE: Busy year ahead for Peptide Therapeutics
SOURCE: Scrip (1998) No. 2371 p13
DOCUMENT TYPE: Newsletter
FILE SEGMENT: FULL

(FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS, TOXLIT, TOXLINE, PHIC, PHIN' ENTERED AT 16:22:37 ON 14 JUN 2000)
L9 4 SEA ABB=ON PLU=ON L6 AND (BACTERIOPHAG? OR BACTER? PHAG? OR PROMOTER)
L10 1 SEA ABB=ON PLU=ON L9 NOT L7

L10 ANSWER 1 OF 1 TOXLIT
ACCESSION NUMBER: 1999:97744 TOXLIT
DOCUMENT NUMBER: CA-131-347498N
TITLE: Cytotoxin-based biological containment system based on protein degradation for environmental pollution clean-up.
AUTHOR: Gerdes K; Gotfredsen M; Gronlund H; Pedersen K; Kristoffersen P
SOURCE: (1999). PCT Int. Appl. PATENT NO. 9958652 11/18/1999 (GXBiosystems A/S).
CODEN: PIXXD2.
PUB. COUNTRY: DENMARK
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 131:347498
ENTRY MONTH: 199912

AB Method of conditionally controlling the survivability of a **recombinant** cell population and of contg. such cells to an environment or contg. replicons to a host cell is based on the use of protein killer systems including the E. coli relBE locus and similar systems found in Gram-neg. (**Enterobacteriaceae**, Hemophilus, Vibrionaceae, Pseudomonadaceae, **Helicobacter**, and Synechosystis) and Gram-pos. bacteria (Bacillaceae and Mycobacterium and Bacillus thuringiensis) and Archaea. Such system are generally based on a cytotoxin polypeptide and an antitoxin or antidote polypeptide that in contrast to the cytotoxin is degradable by proteases. In this system the regulation of the relE gene is stochastically regulated. Here the **promoter** is invertible. This involves flanking the regulatory sequence with repeat sequences where at least part of the regulatory sequence is recombinationally excised. Expression of genes of interest may include an enzyme or an immunol. active peptide or a pesticide or a pharmaceutically active gene product. Methods for post-segregationally stabilizing a plasmid in a microbial host cell involves integration a plasmid with regulated expression of a first kind of protein with a toxic effect and a gene coding for a second kind of polypeptide with an antitoxin effect. This first kind of polypeptide may inhibit translation. The antitoxin is capable of being degraded at a higher rate than the first polypeptide. Screening for daughter cells in employed where one that does not receive at least one copy of the plasmid is killed as a result of faster degrdn. The **recombinant** cells are useful as **vaccines**, pollutant degrading organisms or as biol. pest control organisms e.g. expressing B. thuringiensis cryst. proteins.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS, TOXLIT, TOXLINE, PHIC, PHIN' ENTERED AT 16:24:58 ON 14 JUN 2000)
Searcher : Shears 308-4994

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS, TOXLIT, TOXLINE, PHIC, PHIN' ENTERED AT 16:24:58 ON 14 JUN 2000)

- Author(s)

L11	4872	SEA	ABB=ON	PLU=ON	MEYER T?/AU
L12	2905	SEA	ABB=ON	PLU=ON	HAAS R?/AU
L13	4	SEA	ABB=ON	PLU=ON	ZHENGXIN Y?/AU
L14	647	SEA	ABB=ON	PLU=ON	(GOMEZ DUARTE O? OR GOMEZ O? OR DUARTE O? OR DUARTE GOMEZ O?)/AU
L15	959	SEA	ABB=ON	PLU=ON	LUCAS B?/AU
L16	1	SEA	ABB=ON	PLU=ON	L11 AND L12 AND L13 AND L14 AND L15
L17	145	SEA	ABB=ON	PLU=ON	L11 AND (L12 OR L13 OR L14 OR L15)
L18	6	SEA	ABB=ON	PLU=ON	L12 AND (L13 OR L14 OR L15)
L19	1	SEA	ABB=ON	PLU=ON	L13 AND (L14 OR L15)
L20	6	SEA	ABB=ON	PLU=ON	L14 AND L15
L21	9229	SEA	ABB=ON	PLU=ON	L11 OR L12 OR L13 OR L14 OR L15 OR L17
L22	25	SEA	ABB=ON	PLU=ON	L21 AND L3
L23	25	SEA	ABB=ON	PLU=ON	L16 OR L18 OR L19 OR L20 OR L22
L24	16	DUP REM	L23	(9 DUPLICATES REMOVED)	

L24 ANSWER 1 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 2000:230683 BIOSIS

DOCUMENT NUMBER: PREV200000230683

TITLE: Rapid and specific detection of **Helicobacter** pylori macrolide resistance in gastric tissue by fluorescent in situ hybridisation.

AUTHOR(S): Trebesius, K.; Panthel, K.; Strobel, S.; Vogt, K.; Faller, G.; Kirchner, T.; Kist, M.; Heesemann, J.; **Haas, R. (1)**

CORPORATE SOURCE: (1) Max von Pettenkofer Institute for Hygiene and Medical Microbiology, Pettenkoferstr. 9a, D-80336, Munich Germany

SOURCE: Gut, (May, 2000) Vol. 46, No. 5, pp. 608-614. ISSN: 0017-5749.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background: The development of macrolide resistance in **Helicobacter** pylori is considered an essential reason for failure of antibiotic eradication therapies. The predominant mechanism of resistance to macrolides, particularly clarithromycin, is based on three defined mutations within 23S rRNA, resulting in decreased binding of the antibiotic to the bacterial ribosome. Aim: To develop an rRNA based whole cell hybridisation method to detect **Helicobacter** species in situ within gastric tissue, simultaneously with its clarithromycin resistance genotype. Methods: A set of fluorescent labelled oligonucleotide probes was developed, binding either to H pylori 16S rRNA or 23S rRNA sequences containing specific point mutations responsible for clarithromycin resistance.

Searcher : Shears 308-4994

After hybridisation and stringent washing procedures, labelling of intact single bacteria was monitored by fluorescence microscopy. The new approach was compared with PCR based assays, histology, and microbiological culture. Results: In comparison with the phenotypic resistance measurement by E test, the genotypic clarithromycin resistance correlated perfectly (100%) for 35 H pylori isolates analysed. In a set of gastric biopsy specimens (27) H pylori infection was confirmed by histology (17/27) and correctly detected by whole cell hybridisation. Five clarithromycin resistant strains were identified in gastric tissue specimens directly. Furthermore, non-cultivable coccoid forms of H pylori were easily detectable by whole cell hybridisation. Conclusions: Whole cell hybridisation of rRNA holds great promise for cultivation independent, reliable, and rapid (three hours) genotypic determination of clarithromycin resistance in H pylori. Compared with PCR techniques it is independent of nucleic acid preparations, not prone to inhibition, and allows semi-quantitative visualisation of the bacteria within intact tissue samples.

L24 ANSWER 2 OF 16 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999210725 MEDLINE
DOCUMENT NUMBER: 99210725
TITLE: The **attenuated Salmonella** vaccine approach for the control of **Helicobacter** pylori-related diseases.
AUTHOR: **Gomez-Duarte O G**; Bumann D; **Meyer T F**
CORPORATE SOURCE: Abteilung Infektionsbiologie, Max-Planck-Institut fur Biologie, Tubingen, Germany.
SOURCE: VACCINE, (1999 Mar 26) 17 (13-14) 1667-73. Ref: 81
Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY WEEK: 19990705
AB The Gram-negative bacterium **Helicobacter** pylori is a widespread human **pathogen** that colonizes the gastric mucosa and is associated with gastro-intestinal illnesses such as gastritis, peptic ulcer, gastric lymphoma and gastric cancer. Current pharmacological therapies are becoming less reliable for the control of H. pylori due to the elevated costs and to the increasing number of antibiotic resistant strains. New vaccination strategies utilizing H. pylori antigens combined with adjuvants or delivery of antigens by **attenuated Salmonella** strains have been successful in protecting mice against H. pylori infections.

Searcher : Shears 308-4994

Oral immunization with single doses of **urease**-expressing **Salmonella** vaccine strains elicits mucosal and systemic antibody responses and fully protects different mouse strains against challenge infections with H. pylori. The high efficacy in the mouse model, combined with remarkable immunogenicity, safety and low-cost production, makes **attenuated** live **recombinant Salmonella** promising vaccine candidates for the control of H. pylori-related diseases in humans.

L24 ANSWER 3 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:42193 BIOSIS
DOCUMENT NUMBER: PREV200000042193
TITLE: A plasmid-based vector system for the cloning and expression of **Helicobacter** pylori genes encoding outer membrane proteins.
AUTHOR(S): Fischer, W. (1); Schwan, D.; Gerland, E.; Erlenfeld, G. E.; Odenbreit, S.; **Haas, R.**
CORPORATE SOURCE: (1) Max von Pettenkofer-Institut fuer Hygiene und Medizinische Mikrobiologie, Ludwig-Maximilians-Universitaet, Pettenkoferstr. 9a, D-80336, Muenchen Germany
SOURCE: Molecular and General Genetics, (Oct., 1999) Vol. 262, No. 3, pp. 501-507.
ISSN: 0026-8925.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Helicobacter** pylori produces a number of proteins associated with the outer membrane, including adhesins and the vacuolating cytotoxin. We observed that the functional expression of such proteins is deleterious to Escherichia coli, the host bacterium used for gene cloning. Therefore, a general method was developed for the functional expression of such genes on a shuttle vector in H. pylori, which has been termed SOMPES (Shuttel vector-based Outer Membrane Protein Expression System). The intact, active gene is reconstituted by recombination in H. pylori from partial gene sequences cloned on an E. coli-H. pylori shuttle vector. This system was established in an H. pylori strain carrying a precise, unmarked chromosomal deletion of the vacA gene, which was constructed by adapting the streptomycin sensitivity system to H. pylori. It is based on the expression of the H. pylori rpsL gene as a counterselectable marker in the genetic background of an rpsL mutant. The utility of this approach is demonstrated by the expression of a **recombinant** gene encoding vacuolating cytotoxin (vacA) and a **recombinant** gene encoding an adherence-associated outer membrane protein (**alpA**) in H. pylori.

L24 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 1999:484691 BIOSIS
DOCUMENT NUMBER: PREV199900484691
TITLE: High efficacy of single dose oral vaccination against **Helicobacter** pylori infection with **recombinant attenuated Salmonella**.
AUTHOR(S): Koesling, J. (1); **Gomez-Duarte, O. G. (1)**; Yan, Z. X. (1); **Lucas, B. (1)**; Panthel, K. (1); **Haas, R. (1)**; **Meyer, T. F. (1)**
CORPORATE SOURCE: (1) Max-Planck Institut fuer Infektionsbiologie, Berlin Germany
SOURCE: Gut, (Sept., 1999) Vol. 45, No. SUPPL. 3, pp. A57-A58.
Meeting Info.: XIIth International Workshop on Gastroduodenal Pathology and Helicobacter pylori Helsinki, Finland September 2-4, 1999
ISSN: 0017-5749.
DOCUMENT TYPE: Conference
LANGUAGE: English

L24 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:341583 CAPLUS
DOCUMENT NUMBER: 129:64083
TITLE: **Helicobacter** polypeptides and corresponding polynucleotide molecules for use in vaccination methods to prevent or treat infection
INVENTOR(S): **Haas, Rainer**; Kleanthous, Harold; Tomb, Jean-Francois; Miller, Charles; Al-Garawi, Amal; Odenbreit, Stefan; **Meyer, Thomas** ; et al.
PATENT ASSIGNEE(S): Merieux Oravax Societe en Nom Collectif Pasteur Merieux Serums et Vaccins S., Fr.; Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V. Berlin; Human Genome Sciences, Inc.
SOURCE: PCT Int. Appl., 365 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9821225	A1	19980522	WO 1997-US21353	19971114

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,

Searcher : Shears 308-4994

MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9852662 A1 19980603 AU 1998-52662 19971114
WO 9843478 A1 19981008 WO 1998-US6371 19980401
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9870995 A1 19981022 AU 1998-70995 19980401
EP 977482 A1 20000209 EP 1998-917972 19980401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT,
IE, FI
PRIORITY APPLN. INFO.: US 1996-749051 19961114
US 1997-831309 19970401
US 1997-833457 19970401
US 1997-834705 19970401
US 1997-881227 19970624
US 1997-902615 19970729
WO 1997-US21353 19971114
WO 1998-US6371 19980401

AB The invention provides **Helicobacter** polypeptides that can be used in vaccination methods for preventing or treating **Helicobacter** infection, and polynucleotides that encode these polypeptides. A representative gene library was constructed in Escherichia coli, in which target genes encoding exported H. pylori proteins were efficiently tagged by transposon TnMax9. Sequences of clones using the transposon shuttle mutagenesis methods were used to identify intact genes, lacking inserted transposons, in the H. pylori genome. Methods are also provided for (1) identification of signal sequences and primer design for amplification of genes lacking signal sequences, (2) cloning of H. pylori DNA in a vector that provides a histidine tag and prodn. and purifn. of the resulting His-tagged fusion proteins, (3) cloning DNA encoding the polypeptides of the invention so that they can be produced without His-tags, (4) purifn. of **recombinantly** produced polypeptides, (5) obtaining the nucleic acids of the invention from the deposited clones, and (6) purifn. of **recombinant** H. pylori antigen GHPO 1190. Eighty-five different gene sequences and the deduced amino acid sequences of their encoded proteins are provided.

Searcher : Shears 308-4994

L24 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:251195 CAPLUS
DOCUMENT NUMBER: 128:307520
TITLE: **Helicobacter** pylori live vaccine
INVENTOR(S): **Meyer, Thomas F.; Haas, Rainer ; Zhengxin, Yan; Gomez-Duarte, Oscar; Lucas, Bernadette**
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V., Germany; Meyer, Thomas F.; Haas, Rainer; Zhengxin, Yan; Gomez-Duarte, Oscar; Lucas, Bernadette
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816552	A1	19980423	WO 1997-EP4744	19970901
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 835928	A1	19980415	EP 1996-116337	19961011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
EP 931093	A1	19990728	EP 1997-940148	19970901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, FI				
BR 9713254	A	19991103	BR 1997-13254	19970901
NO 9901692	A	19990604	NO 1999-1692	19990409
PRIORITY APPLN. INFO.:			EP 1996-116337	19961011
			WO 1997-EP4744	19970901

AB The present invention relates to novel **recombinant** live vaccines, which provide protective immunity against an infection by **Helicobacter** pylori and a method of screening H. pylori antigens for optimized vaccines. Thus, **Salmonella** typhimurium expressing ureA/ureB subunits of **Helicobacter** pylori was constructed and used as vaccine to elicit protective immunity against H. pylori infection.

L24 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
Searcher : Shears 308-4994

ACCESSION NUMBER: 1998:67768 CAPLUS
DOCUMENT NUMBER: 128:166045
TITLE: Mice are protected from **Helicobacter** pylori infection by nasal immunization with **attenuated Salmonella** typhimurium phoPc expressing **urease** A and B subunits
AUTHOR(S): Corthesy-Theulaz, Irene E.; Hopkins, Sally; Bachmann, Daniel; Saldinger, Pierre F.; Porta, Nadine; **Haas, Rainer**; Zheng-Xin, Yan; **Meyer, Thomas**; Bouzourene, Hanifa; Blum, Andre L.; Kraehenbuhl, Jean-Pierre
CORPORATE SOURCE: Division of Gastroenterology, Department of Internal Medicine CHUV, Lausanne, CH-1011, Switz.
SOURCE: Infect. Immun. (1998), 66(2), 581-586
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Live **Salmonella** typhimurium phoPc bacteria were tested as mucosal vaccine vectors to deliver **Helicobacter** pylori antigens. The genes encoding the A and B subunits of H. pylori **urease** were introduced into S. typhimurium phoPc and expressed under the control of a constitutive tac promoter (tac-ureAB) or a two-phase T7 expression system (cT7-ureAB). Both **recombinant Salmonella** strains expressed the two **urease** subunits in vitro and were used to nasally immunize BALB/c mice. The plasmid carrying cT7-ureAB was stably inherited by bacteria growing or persisting in the spleen, lungs, mesenteric or cervical lymph nodes, and Peyer's patches of immunized mice, while the plasmid carrying tac-ureAB was rapidly lost. Spleen and Peyer's patch CD4+ lymphocytes from mice immunized with S. typhimurium phoPc cT7-ureAB proliferated in vitro in response to **urease**, whereas cells from mice given S. typhimurium phoPc alone did not. Splenic CD4+ cells from mice immunized with phoPc cT7-ureAB secreted gamma interferon and interleukin 10, while Peyer's patch CD4+ cells did not secrete either cytokine. Specific H. pylori anti-**urease** IgG1 and IgG2a antibodies were detected following immunization, confirming that both Th1- and Th2-type immune responses were generated by the live vaccine. Sixty percent of the mice (9 of 15) immunized with S. typhimurium phoPc cT7-ureAB were resistant to infection by H. pylori, while all mice immunized with phoPc tac-ureAB (15 of 15) or phoPc (15 of 15) were infected. The data demonstrate that H. pylori **urease** delivered nasally by using a vaccine strain of S. typhimurium can trigger Th1- and Th2-type responses and induce protective immunity against **Helicobacter** infection.

L24 ANSWER 8 OF 16 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998152200 MEDLINE
DOCUMENT NUMBER: 98152200
TITLE: Protection of mice against gastric colonization by **Helicobacter** pylori by single oral dose immunization with **attenuated Salmonella** typhimurium producing **urease** subunits A and B.
AUTHOR: **Gomez-Duarte O G**; **Lucas B**; Yan Z X; Panthel K; **Haas R**; **Meyer T F**
CORPORATE SOURCE: Max-Planck-Institut fur Biologie, Abteilung Infektionsbiologie, Tubingen, Germany.
SOURCE: VACCINE, (1998 Mar) 16 (5) 460-71. Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY WEEK: 19980603

AB **Helicobacter** pylori is a Gram-negative bacterial **pathogen** associated with gastritis, peptic ulceration, and gastric carcinoma. The bacteria express a strong **urease** activity which is known to be essential for colonization of gnotobiotic pigs and nude mice. UreA and UreB, two structural subunits of the active enzyme, were expressed in the **attenuated Salmonella** typhimurium live vaccine SL3261 strain. Evaluation of protection against H. pylori was performed in Balb/c mice by oral immunization with a single dose of the vaccine strain. Five weeks after immunization, mice were challenged orally three times with a mouse-adapted H. pylori wild type strain and, six weeks later, mice were sacrificed to determine H. pylori infection by detection of **urease** activity from the antral region of the mouse stomachs. In several independent experiments, we observed 100% infection with H. pylori in the non-immunized mice and no infection (100% protection) in the mice immunized with S. typhimurium expressing **recombinant** UreA and UreB. Specific humoral and mucosal antibody responses against UreA and UreB were observed in mice immunized as indicated by western blots and ELISA assays. These data shows that oral immunization of mice with **urease** subunits delivered by an **attenuated Salmonella** strain induced a specific immune response and protected mice against H. pylori colonization. Single oral dose immunization with UreA and UreB delivered by a live **Salmonella** vaccine vector appears to be an attractive candidate for human vaccination against H. pylori infection. In addition, this model will aid to elucidate the effective protection mechanisms against H. pylori in the gastric mucosa.

Searcher : Shears 308-4994

L24 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:640781 CAPLUS
DOCUMENT NUMBER: 127:315572
TITLE: **Recombinant** protein fusion products presentation on bacteria cell surface and release by proteinase
INVENTOR(S): Maurer, Jochen; Jose, Joachim; **Meyer, Thomas F.**
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V., Berlin, Germany; Maurer, Jochen; Jose, Joachim; Meyer, Thomas F.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735022	A1	19970925	WO 1996-EP1130	19960315
W: AU, CA, CN, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2248754	AA	19970925	CA 1996-2248754	19960315
AU 9651097	A1	19971010	AU 1996-51097	19960315
AU 714389	B2	19991223		
EP 886678	A1	19981230	EP 1996-907487	19960315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1216065	A	19990505	CN 1996-180254	19960315
JP 2000504928	T2	20000425	JP 1997-519186	19960315
PRIORITY APPLN. INFO.:			WO 1996-EP1130	19960315

AB The present invention relates to vectors, host-vector combinations and processes for producing stable fusion proteins consisting of a carrier protein and a passenger protein. Expression of the fusion protein results in exposure of the passenger domains on the surface of bacterial cells, in particular Escherichia coli. If necessary, the passenger domains can be released into the medium by proteases, e.g. by selected host factors such as OmpT.

L24 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:252329 BIOSIS
DOCUMENT NUMBER: PREV199799551532
TITLE: MALT-type lymphoma of the stomach is associated with **Helicobacter** pylori strains expression the CagA protein.
AUTHOR(S): Eck, Matthias (1); Schmausser, Bernd; **Haas, Rainer**; Greiner, Axel; Czub, Stefanie;

Mueller-Hermelink, Hans Konrad
CORPORATE SOURCE: (1) Institut fuer Pathologie, Universitaet Wuerzburg, Josef-Schneider Strasse 2, D-97080 Wuerzburg Germany
SOURCE: Gastroenterology, (1997) Vol. 112, No. 5, pp. 1482-1486.
ISSN: 0016-5085.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Background & Aims: **Helicobacter** pylori is considered to be involved in the pathogenesis of gastric lymphoma of mucosa-associated lymphoid tissue (MALT) type. Strains expressing the CagA protein (CagA+ strains) have been strongly associated with severe gastritis, duodenal ulceration, and gastric adenocarcinoma. The aim of this study was to determine the presence of H. pylori as well as incidence of CagA+ strains in gastric MALT-type lymphoma. Methods: Sera of 68 patients with gastric MALT-type lymphoma (22 with low grade, 36 with high grade, and 10 with secondary high grade) were obtained, and the serological response to CagA was studied by immunoblotting using a purified **recombinant** CagA protein, a CagA+ strain, and the corresponding isogenic CagA- mutant. Results: Of the patients with MALT-type lymphoma, 98.5% (67 of 68 patients) were H. pylori seropositive. In the only seronegative patient, the bacterium was detected histologically by Warthin-Starry staining. Of the seropositive patients, 95.5% had serum immunoglobulin G antibodies to CagA compared with 67% of an H. pylori-positive control group (33 of 49 patients; P = 0.000037) with chronic active gastritis. Conclusions: These results indicate infection of almost all patients with MALT-type lymphoma by CagA+ H. pylori strains. Strains expressing the CagA protein seem to play a crucial role in the pathogenesis of gastric MALT-type lymphoma.

L24 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:530603 CAPLUS
DOCUMENT NUMBER: 127:204061
TITLE: Vaccine development against **Helicobacter** pylori infections
AUTHOR(S): **Haas, Rainer; Meyer, Thomas F.**
CORPORATE SOURCE: Max-Planck-Institut fur Biologie, Abteilung Infektionsbiologie, Tubingen, D-72076, Germany
SOURCE: Biologicals (1997), 25(2), 175-177
CODEN: BILSEC; ISSN: 1045-1056
PUBLISHER: Academic
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 13 refs. Topics discussed include: animal models for vaccine development, identification of H. pylori antigens providing protection against **Helicobacter** infection, prophylactic and therapeutic immunization strategies, the basis of protective immunity, new strategies to identify further efficient vaccine

candidates, and use of **attenuated Salmonella** strains as live vaccine carriers for H. pylori antigens.

L24 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:25674 BIOSIS
DOCUMENT NUMBER: PREV199800025674
TITLE: **Urease** subunits A and B delivered by **attenuated Salmonella** typhimurium vaccine strain protects mice against gastric colonization by **Helicobacter** pylori.
AUTHOR(S): **Gomez-Duarte, O. G.**; Yan, Z. X.; **Lucas, B.**; Panthel, K.; **Haas, R.**; **Meyer, T. F.**
CORPORATE SOURCE: Max-Planck Inst. Biologie, Tuebingen Germany
SOURCE: Gut, (1997) Vol. 41, No. SUPPL. 1, pp. A59-A60. Meeting Info.: European Helicobacter Pylori Study Group Xth International Workshop on Gastroduodenal Pathology and Helicobacter Pylori Lisbon, Portugal September 11-14, 1997 European Helicobacter pylori Study Group . ISSN: 0017-5749.
DOCUMENT TYPE: Conference
LANGUAGE: English

L24 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1995:532850 BIOSIS
DOCUMENT NUMBER: PREV199598547150
TITLE: Cloning of the **Helicobacter** pylori recA gene and functional characterization of its product.
AUTHOR(S): Schmitt, Wolfgang; Odenbreit, Stefan; Heuermann, Dorothee; **Haas, Rainer**
CORPORATE SOURCE: Max-Planck-Inst. Biol., Abt. Infektionsbiol., Spemannstr. 34, D-72076 Tuebingen Germany
SOURCE: Molecular & General Genetics, (1995) Vol. 248, No. 5, pp. 563-572. ISSN: 0026-8925.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The RecA protein is a key enzyme involved in DNA recombination in bacteria. Using a polymerase chain reaction (PCR) amplification we cloned a recA homolog from **Helicobacter** pylori. The gene revealed an open reading frame (ORF) encoding a putative protein of 37.6 kDa showing closest homology to the Campylobacter jejuni RecA (75.5% identity). A putative ribosome binding site and a near-consensus sigma-70 promoter sequence was found upstream of recA. A second ORF, encoding a putative protein with N-terminal sequence homology to prokaryotic and eukaryotic enolases, is located directly downstream of recA. Compared to the wild-type strains, isogenic H. pylori recA deletion mutants of strains 69A and

NCTC11637 displayed increased sensitivity to ultraviolet light and abolished general homologous recombination. The **recombinant** H. pylori RecA protein produced in Escherichia coli strain GC6 (recA-) was 38 kDa in size but inactive in DNA repair, whereas the corresponding protein in H. pylori 69A migrated at the greater apparent molecular weight of approx. 40 kDa in SDS-polyacrylamide gels. However, complementation of the H. pylori mutant using the cloned recA gene on a shuttle vector resulted in a RecA protein of the original size and fully restored the general functions of the enzyme. These data can be best explained by a modification of RecA in H. pylori which is crucial for its function. The potential modification seems not to occur when the protein is produced in E. coli, giving rise to a smaller but inactive protein.

L24 ANSWER 14 OF 16 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 95011230 MEDLINE
DOCUMENT NUMBER: 95011230
TITLE: Immunization of BALB/c mice against **Helicobacter** felis infection with **Helicobacter** pylori **urease**.
AUTHOR: Michetti P; Corthesy-Theulaz I; Davin C; **Haas R**; Vaney A C; Heitz M; Bille J; Kraehenbuhl J P; Saraga E; Blum A L
CORPORATE SOURCE: Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland..
SOURCE: GASTROENTEROLOGY, (1994 Oct) 107 (4) 1002-11. Journal code: FH3. ISSN: 0016-5085.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199501
AB BACKGROUND/AIMS: Because **Helicobacter** pylori is a potentially dangerous human **pathogen**, the protective potential of oral immunization with H. pylori **urease** and its subunits was evaluated in an animal model. METHODS: Mice were orally immunized with H. pylori sonicate, **urease**, or **recombinant** enzymatically inactive **urease** subunits and then challenged with **Helicobacter** felis. Control mice were sham-immunized. RESULTS: H. felis colonization was present 5 days after challenge in 9 of 10 sham-immunized, 6 of 9 sonicate-immunized, and 3 of 10 **urease**-immunized animals (P = 0.031 vs. sham-immunized). Twelve days after challenge, **urease** B-immunized mice had a weaker colonization than sham-immunized controls, whereas **urease** A had no effect. After 70 days, most **urease** A- and **urease** B-immunized mice had cleared the colonization (10/17: P = 0.0019; 16/20: P = 0.00002 vs. sham-immunized). In **urease**

B-immunized animals, protection was often associated with corpus gastritis. CONCLUSIONS: Oral immunization with H. pylori **urease** protects mice against H. felis infection. Enzymatically inactive **urease** A and B subunits contain protective epitopes. It is unclear whether protection depends on the development of a mononuclear inflammatory response in the gastric corpus. Our observations should encourage the development of a human vaccine.

L24 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1993:389645 BIOSIS
DOCUMENT NUMBER: PREV199396064945
TITLE: Aflagellated mutants of **Helicobacter** pylori generated by genetic transformation of naturally competent strains using transposon shuttle mutagenesis.
AUTHOR(S): **Haas, Rainer (1)**; **Meyer, Thomas F.** ; Van Putten, Jos P. M.
CORPORATE SOURCE: (1) Max-Planck-Inst. Biologie, Abteilung Infektionsbiologie, Spemannstrasse 34, D-7400 Tuebingen Germany
SOURCE: Molecular Microbiology, (1993) Vol. 8, No. 4, pp. 753-760.
ISSN: 0950-382X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Three out of 10 **Helicobacter** pylori clinical isolates were found to be naturally competent for genetic transformation to streptomycin resistance by chromosomal DNA extracted from a spontaneous streptomycin-resistant H. pylori mutant. The frequency of transformation varied between 5 times 10-4 and 4 times 10-6, depending on the H. pylori isolate used. Transposon shuttle mutagenesis based on this natural competence was established using the flagellin gene flaA as the target. The cloned flaA gene was interrupted by insertion of TnMax1, a mini-Tn1721 transposon carrying a modified chloramphenicol-acetyltransferase gene, the cat-GC cassette. Natural transformation of competent H. pylori strains with plasmid constructs harbouring a cat-GC-inactivated flaA gene resulted in chloramphenicol-resistant transformants at an average frequency of 4 times 10-5. Southern hybridization experiments confirmed the replacement of the chromosomal H. pylori flaA gene by the cat-inactivated cloned gene copy via homologous recombination resulting in allelic exchange. Phenotypic characterization of the mutants demonstrated the absence of flagella under the electron microscope and the loss of bacterial motility. Immunoblots of cell lysates of the H. pylori mutants with an antiserum raised against the C-terminal portion of **recombinant** H. pylori major flagellin (FlaA) confirmed the absence of the 54 kDa FlaA protein. This efficient transposon

shuttle mutagenesis procedure for H. pylori based on natural competence opens up new possibilities for the genetic assessment of putative H. pylori virulence determinants.

L24 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1993:4056 BIOSIS
DOCUMENT NUMBER: PREV199395004056
TITLE: Cloning and genetic characterization of a **Helicobacter** pylori flagellin gene.
AUTHOR(S): Leying, H.; Suerbaum, S.; Geis, G.; **Haas, R.** **(1)**
CORPORATE SOURCE: (1) Max-Planck-Inst. Biol., Abt. Infektionsbiol., Spemannstrasse 34, D-7400 Tuebingen Germany
SOURCE: Molecular Microbiology, (1992) Vol. 6, No. 19, pp. 2863-2874.
ISSN: 0950-382X.
DOCUMENT TYPE: Article
LANGUAGE: English

AB **Helicobacter** pylori produces polar sheathed flagella, which are believed to be essential for the bacterial colonization of the human gastric mucosa. Here we report on the cloning and genetic characterization of a H. pylori gene encoding the subunit of the flagellar filament, the flagellin. Screening of a genomic library of H. pylori with an oligonucleotide probe derived from the N-terminal amino acid sequence of purified flagellin resulted in a **recombinant**-plasmid clone carrying the flagellin-encoding gene flaA on a 9.3 kb BglII fragment. The nucleotide sequence of flaA revealed an open reading frame of 1530 nucleotides, encoding a protein with a predicted molecular mass 53.2 kDa, which is similar in size with the purified flagellin protein in SDS-polyacrylamide gel electrophoresis. Sequence alignment of H. pylori flagellin (FlaA) with other bacterial flagellins demonstrates a high degree of similarity in the amino-terminal and carboxy-terminal regions, including those of the closely related genus Campylobacter (56% overall identity with Campylobacter Coli flaA), but little homology in the central domain. Southern hybridization of chromosomal DNA with flaA-specific probes did not reveal the presence of addtional homologous flagellin genes in H. pylori. Sequence analysis of flaA flanking regions and mapping of the flaA mRNA start site b a primer extension experiment indicated that transcription of the gene is under the control of a sigma-28-specific promoter sequence in H. pylori. The region upstream of the flaA promoter is subject to local DNA modification, resulting in the masking of two out of three closely linked HindIII restriction sites in the chromosome of strain 898-1. Escherichia coli strains harbouring the **recombinant** plasmid did not produce full-length flagellin and data obtained with FlaA fusion proteins using an E. coli plasmid expression system suggest that a distinct nucleotide sequence in the gene interferes with productive translation of this protein in E. coli.

Searcher : Shears 308-4994